

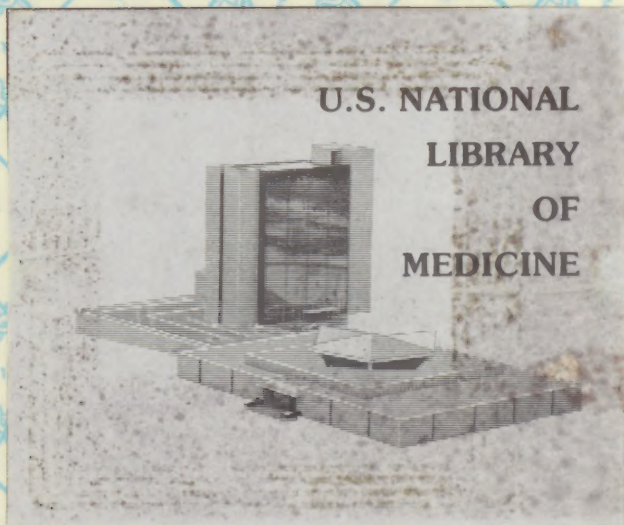
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ESSENTIALS
OF
PHYSIOLOGY

PREPARED ESPECIALLY FOR
STUDENTS OF MEDICINE

BY
SIDNEY P. BUDGETT, M.D.

Formerly Professor of Physiology in the Medical Department of Washington
University, St. Louis.

Fourth Edition, Thoroughly Revised

BY
HAROLD E. B. PARDEE, M.D.

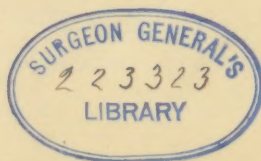
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ARRANGED WITH QUESTIONS FOLLOWING EACH CHAPTER

ILLUSTRATED

PHILADELPHIA AND LONDON
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PREFACE TO THE FOURTH EDITION

It has been thought advisable to collect many of the fundamental facts into an introductory paragraph, and to change the order in which the various physiologic systems were considered. Much new material has been introduced, such as the physics of electric stimulation, the chemistry and physiology of the amino-acids, the galvanometric method of recording electric phenomena, the source and classification of the leukocytes, and many new facts in relation to the circulation, including electrocardiography, venous pulse, etc. An endeavor has been made to touch upon as many important facts as space allowed, even though at times they are not treated in great detail.

HAROLD E. B. PARDEE.

NEW YORK, *October, 1915.*

PREFACE.

THESE abbreviated lecture notes are intended for the use of students in conjunction with a text-book, and not as a substitute for a larger work. Consequently, no attempt has been made fully to illustrate this book. The questions introduced at the end of each chapter are not exhaustive, but may, it is hoped, if carefully considered, be found useful as an aid to thinking over what has been read.

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ESSENTIALS OF PHYSIOLOGY

CHAPTER I

INTRODUCTION

PHYSIOLOGY being the study of the functions of protoplasm, we are attempting more and more to explain these functions in terms of the more fundamental sciences of **Physics** and **Chemistry**. There lies, however, beyond our ultimate effort in this direction, a basic fact unexplainable by any knowledge in our possession—the fact which we call **Life**. Life is responsible for the reactions of protoplasm to the various conditions to which it may be subjected, and till we can speak of this in the terms of the basic sciences we can go no further than to say that the *protoplasm* of which the body tissues are composed *shows certain characteristics*. Taken together, these characteristics illustrate the various types of functional activity of which protoplasm is capable.

Irritability is that quality by virtue of which tissues may be caused to functionate by factors outside of themselves. At times this may result in a rhythmic activity.

Rhythmicity is the ability of tissues to originate activity within themselves. This usually occurs intermittently, and usually at a quite constant interval, so that the rhythm is regular.

Conductivity is the ability to transfer activity from one point to another within the tissue involved.

Contractility is the ability of tissue to change its form.

Secretion is the ability to produce substances within the tissue which are for a definite purpose in connection with the life of the organism.

Absorption is the ability to take up into itself substances which are in the surrounding medium.

Nutrition is the ability to use the absorbed substances to carry on the activity of the tissue.

Growth and **repair** depend upon the ability to construct new material from absorbed substances, in order to increase the bulk or to renew the worn-out parts of tissue.

Reproduction is the ability to originate a new protoplasmic unit of the same type which shall survive after the destruction of the original.

The tissues show these characteristics by virtue of life, but the energy necessary is obtained from the food by chemical processes. The chemistry of the tissues is spoken of as **Metabolism**. **Anabolism** is the process of building up more complex bodies, as the protein and fat of tissue from the simpler bodies which occur in the blood after digestion. **Catabolism** is the process of breaking down the more complex bodies, as it takes place in digestion and in the tissue oxidations.

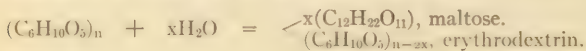
Anything which causes a tissue to functionate is called a **stimulus**. Each tissue has its special type of *natural stimulus*, the most frequent perhaps being a *nerve impulse*. Certain *chemical bodies* act as natural stimuli, as CO_2 to the respiratory center, and the gastric and pancreatic secretins to their respective glands. Chemical bodies such as the latter, formed in one tissue, absorbed into the blood, carried thus to another tissue and causing the second tissue to functionate, are called **hormones**. Many sorts of influences can be applied experimentally to tissues and will cause them to function. These are called *artificial stimuli*, and may be mechanical, thermal, chemical, or electric. As to the *electric current*: the make or the break of the galvanic or battery current acts as a stimulus, but not the flow. On making the current the stimulus starts at the cathode—the electrode connected with

the negative pole of the battery; on breaking the current the stimulus arises at the anode, which is connected with the positive pole. The cathodal stimulus is stronger than the anodal. The flow of current is, of course, from positive to negative pole. The induced or faradic current is stronger on breaking the circuit in the primary coil than on making it, so that the "break shock" will, of course, be the stronger stimulus; some tissues react more readily to the galvanic current, but most react best to the faradic.

It is necessary to have clearly in mind certain **chemical facts** in order to correctly understand the processes of metabolism.

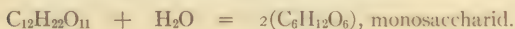
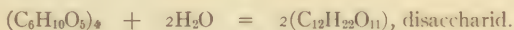
Carbohydrates are organic chemical substances containing carbon, hydrogen, and oxygen atoms, the hydrogen atoms being double the oxygen in number. Glucose (dextrose) may be used as an example, having the formula $C_6H_{12}O_6$ [$CH_2OH(CHOH)_4CHO$]. Carbohydrates having this general formula are called monosaccharids. If two such molecules are joined together and one molecule of water removed, we have the general formula for the disaccharids, $C_{12}H_{22}O_{11}$. Combinations of four or more monosaccharid molecules, with the removal of one molecule of water for each added saccharid, produces a substance called a polysaccharid, with the formula $(C_6H_{10}O_5)_n$. The formation of polysaccharids from monosaccharids is thus seen to be a synthesis, with water as a by-product. This occurs in the body when the dextrose of the blood is converted to glycogen. In glycogen the value of "n" is relatively small, but probably over 10.

The opposite type of process results from the action of the digestive ferments. Starch, a polysaccharid with a very large molecule ($n = 25$, at least), being hydrolyzed repeatedly and reduced ultimately to monosaccharids.



Erythrodextrin is also a polysaccharid; it gives a red color when treated with iodine. The hydrolysis progresses with the

production of maltose, and after many molecules of maltose have been split off, the polysaccharid no longer gives any color with iodine and is called *achroödextrin*. It has the same formula as other polysaccharids except that n has a smaller value. When the value of n is reduced to 4, the substance is called *maltodextrin*. It will reduce Fehling's solution as the mono- and disaccharids. Its hydrolysis may be represented as follows:



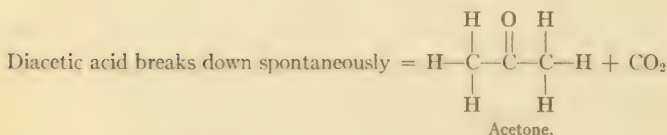
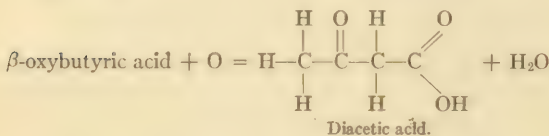
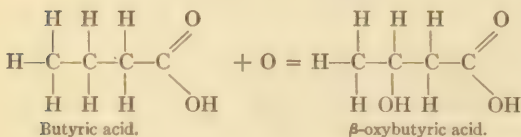
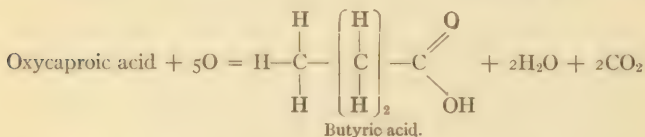
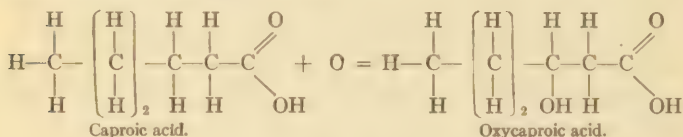
The different disaccharids produce different monosaccharids when hydrolyzed: Maltose = Dextrose + Dextrose. Sucrose = Dextrose + Levulose. Lactose = Dextrose + Galactose.

The steps of the oxidation of the monosaccharid molecule are not known, but lactic acid ($C_3H_6O_3$) appears when glucose is oxidized, as do certain more complex oxyacids, like glycuronic ($C_6H_{10}O_7$), saccharic ($C_6H_{10}O_8$), and oxalic ($C_2H_2O_4$). We are certain that the final products are CO_2 and H_2O .

Fats are much more complex bodies, composed by the union of one molecule of glycerin and three long-chain oxyacids each combined with a CH_3 group. *Palmitin* is a type of such a substance, with the formula $C_3H_5(OCO(CH_2)_{14}CH_3)_3$. Such a substance could be synthesized from carbohydrate radicles, and this synthesis probably occurs in the body. The digestive enzymes hydrolyze these substances, breaking them up into glycerin, ($C_3H_5(OH)_3$), and the fatty acid. Oleic acid, $COOH(CH_2)_{14}(CH)_2CH_3$, and stearic acid, $COOH(CH_2)_{16}CH_3$, are obtained from the fats *olein* and *stearin*, which together with *palmitin* make up the major part of the fats occurring in the body. Human fat is from 67 to 80 per cent. olein, and is liquid at body temperatures.

The further steps in the oxidation of the fatty acids are not known, but we do know that CO_2 and water are the end-products. When a large amount of fat is oxidized, certain

substances appear in the blood which are believed to be the result of incomplete oxidation. They are believed to be present normally in such small amounts at one time as to be inappreciable. The fatty acids are oxidized beginning with the carbon in the β position:



Acetone, diacetic acid, and β -oxybutyric acid all appear in the blood and urine when the fat of the body is called upon to excess, and are known as the *acetone bodies*. It is noticed that only the fatty acids having an even number of carbon atoms could produce these substances.

Fat-like bodies, **lipoids**, also occur, of which the important ones are cholesterin and lecithin. *Cholesterin* is especially abundant in the myelin of the nervous system, but is widely distributed in the tissues. Its formula is $(\text{CH}_3)_2\text{C}_{24}\text{H}_{38}\text{CHOH}$ and it has been shown to belong to the "terpene" group. *Lecithin* contains about 4 per cent. of phosphorus. Its molecule contains five radicles in combination: glycerophosphoric acid, $\text{CH}_2\text{OH}.\text{CHOH}.\text{CH}_2\text{OPO}(\text{OH})_2$, a nitrogenous base called cholin, $(\text{CH}_3)_3\text{N}(\text{CH}_2)_2(\text{OH})_2$, and two molecules of the higher fatty acids, *i. e.*, stearic, oleic, or palmitic. Lecithin, too, occurs chiefly in the myelin of the nervous system, but also is widely distributed.

Proteins, or albumins, are still more complex bodies containing carbon, hydrogen, oxygen, nitrogen, usually sulphur, and often phosphorus or iron. They are formed by the tissues from the products of digestion, and constitute the most characteristic chemical feature of protoplasm. When decomposed by proteolytic enzymes or by boiling with acids, proteins break up with the formation of a number of simpler bodies called **amino-acids**. They are really amino-fatty-acids, being fatty acids in which one or more of the H atoms of the CH_2 groups are replaced by a NH_2 radicle. *Glycocoll* (glycin) is a very simple member of this group, its formula being $\text{CH}_2\text{NH}_2\text{COOH}$. It has only one amin group. Poly-amino-acids also occur, such as *lysin*, which has the formula $\text{NH}_2(\text{CH}_2)_4\text{CHNH}_2\text{COOH}$ and is seen to contain two amin groups.

These bodies can act as acids through the NH_2 group, or as bases through the OH group. Some of them are polybasic as aspartic acid, which has the formula $\text{COOHCH}_2\text{CHNH}_2\text{COOH}$. The amino bodies can join together by the union of the OH group of one with the amin group of the other, giving off one molecule of water, and it seems very likely that this is the way they are joined in the protein molecule. The product of such a union is called a *peptid*.

The organism is capable of synthesizing some of these bodies, glycocoll, for example, but others, as tyrosin, C_6H_4 -

$\text{OHCH}_2\text{CHNH}_2\text{COOH}$, and lysin, it cannot produce itself. About twenty-five amino-acids have been isolated, but not every protein molecule contains them all. The varied percentage composition of five typical proteins appears from the table (Fig. 1).

	Serum albumin.	Serum globulin.	Casein.	Ovalbumin.	Gliadin.
Glycin.....		3.5			
Alanin.....	2.7	2.2	1.5	2.2	2.0
Valin.....		Present	77.2	2.5	3.3
Leucin.....	20.0	18.7	9.3	10.7	6.6
Prolin.....	1.0	2.8	6.7	3.6	13.2
Oxyprolin.....			0.2	?	?
Phenylalanin....	3.1	3.8	3.2	5.0	2.3
Glutaminic acid..	7.7	8.5	15.5	9.1	43.6
Aspartic acid....	3.1	2.5	1.4	2.2	0.6
Serin.....	0.6		0.5	?	0.1
Tyrosin.....	2.1	2.5	4.5	1.7	1.6
Cystin.....	2.3	0.7	?	?	0.5
Histidin.....			2.5	1.7	1.5
Arginin.....			3.8	4.9	2.9
Lysin.....			5.9	3.7	0.1
Tryptophan.....	Present	Present	1.5	Present	1.0

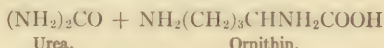
Fig. 1.—Table of proteins.

The figures will not add up to 100 per cent. because there are amino bodies which we cannot as yet recognize.

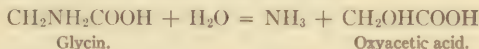
Some proteins also contain in their molecule a carbohydrate radicle, being called *glycoproteins*. Mucin is a type. *Nucleo-proteins* are combinations of protein with nucleic acid, which is itself a phosphoric acid, nitrogenous base, carbohydrate compound. Protein combines with lecithin to form *lecitho-protein*, and with another phosphorus-containing substance, not nucleic acid or lecithin, to form *phosphoprotein*. Vitellin of egg-yolk and casein of milk are such. *Chromoproteins* or hemoglobins are a combination of protein with a pigment grouping (see under Blood). Various other classifications are based on solubility and have little physiologic signifi-

cance. Albumin, proteose, and peptone are soluble in water; globulin and albuminate are soluble in alkaline media, as are also the other three; proteose and peptone alone are diffusible.

The catabolic changes which the amino-acids undergo are very complicated. Polyamino-acids are hydrated with splitting off of urea, $(\text{NH}_2)_2\text{CO}$:



Monamino-acids result in ammonia—



Ammonia is converted to ammonium carbonate by the blood alkali, and this, in turn, is largely converted by the liver to urea:

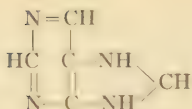


The fatty acid radicles left after the deaminization may be oxidized as described, or may be synthesized to form carbohydrate.

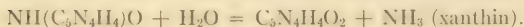
The further steps in the oxidation of *nucleoprotein* are of considerable importance physiologically. The enzyme nuclease acts upon the nucleic acid radicle after it has been split from the protein, and the nitrogenous bases *adenin* and *guanin* are the important substances which are obtained. Both of these bodies contain a nucleus represented by



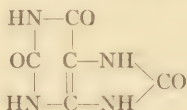
which is called the purin nucleus (C_5N_4). The hydrogen compound of this would be purin ($\text{C}_5\text{N}_4\text{H}_4$):



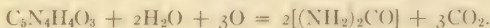
Adenin and guanin are amino-purins, $\text{NH}(\text{C}_5\text{N}_4\text{H}_4)$ being adenin, and $\text{NH}(\text{C}_5\text{N}_4\text{H}_4)\text{O}$ being guanin. The enzymes adenase and guanase deamidize them, producing hypoxanthin and xanthin respectively:



These products are acted on by an oxydase; hypoxanthin is converted to xanthin, and this to uric acid ($\text{C}_5\text{N}_4\text{H}_4\text{O}_3$):



About one-half of the uric acid formed is, in turn, split by a uricolytic enzyme, so that its N is eliminated as urea:



Enzymes are chemical substances containing nitrogen and usually sulphur, but are probably not protein in nature. Their importance lies in the fact that they produce or accelerate many of the important processes of the body. They are not used up by this, but act as catalytic agents. They are destroyed by temperatures of 60° to 80° C. and their activity is retarded or stopped by low temperatures. Enzymes are often secreted in an inactive form called **Zymogen**, which, on contact with a second substance, is changed to the enzyme. This second substance is said to *activate* the zymogen, and is called an *activator* if inorganic, or *kinase* if organic. Pepsin and trypsin are both secreted in an inactive form.

Enzyme action is reversible; that is, if an enzyme can break down a substance into its components, it is able also to synthesize the components to form the more complex body; also the enzyme action is checked when a certain concentration of the end-products is reached. This seldom occurs in the body, for the end-products are continually removed, but it may occur under experimental conditions.

The nomenclature of enzymes is usually based upon the substance on which they act, but those which were discovered earlier have retained their special names. *Proteolytic* enzymes, acting on proteins and causing a hydrolytic cleavage, are pepsin, trypsin, erepsin. *Amylolytic* enzymes, acting on starch and causing a hydrolytic cleavage, are ptyalin, amyl-opsin, the diastase of liver and muscle. *Inverting* enzymes, acting on disaccharids and converting them to monosaccharids, are maltase, invertase, lactase. *Lipolytic* enzymes, acting on fats and causing a hydrolytic cleavage, are steapsin and the lipase of liver and the tissues generally. *Oxidizing* enzymes, acting on the monosaccharids and on the oxyacid radicles of the amino bodies and the fatty acids, oxidizing them through various stages to CO_2 and water, are called oxydases. *Deamidizing* enzymes, which split off the amin (NH_2) group from the amino bodies in the form of ammonia or of urea, are named from the substance on which they act, adenase, guanase, arginase, etc. There are also certain special enzymes: as *nuclease*, which splits nucleic acid; *urease*, which converts ammonium salts to urea, etc.

Calorimetry.—It is noticed that the catabolic changes are all oxidative, and they accordingly give off heat to the body. When any substance is burned in a suitable instrument the heat produced may be measured. The instrument is called a **Calorimeter**. The unit of measurement for heat is called a calorie; it is the amount of heat which will raise 1 gram of water 1°C . In physiologic work the large calorie, abbreviated C., is usually used, and is equal to 1000 calories. The results as to heat obtained by burning the carbohydrates and fats in a calorimeter correspond very well

with the results of feeding them to an animal and determining the amount of heat or energy liberated in the animal's body by means of a calorimeter of large enough dimensions. Proteins, however, give a much larger value when burned directly than when administered as food to an animal. This is readily understood, since urea, the chief end-product of protein metabolism, is still capable of further oxidation, as are also the purin bases, creatinin, etc. The fuel value to the body (**Caloric Value**) of the three types of food-stuffs has been determined as follows, per gram of dried substance:

Carbohydrate.....	4100 calories (4.1 C.)
Fat.....	9300 calories (9.3 C.)
Protein.....	4100 calories (4.1 C.)

though by direct oxidation in a calorimeter protein will give off 5778 calories per gram.

Osmosis is an important feature of physiologic processes. Its nature is not thoroughly understood, but it is in a manner related to the tendency of two gases placed in the same container to diffuse throughout the container and form a uniform mixture. The molecules of salts in solution have this same tendency to form a uniform mixture. Molecules of liquids and of salts in solution are able to pass through the interstices of animal membrane, so that if two solutions be separated by a membrane the molecules will pass across from one side to the other, and ultimately a uniform mixture will be produced. This process of diffusion through a membrane is called **osmosis** when liquid molecules are considered, and **dialysis** when speaking of salts in solution. It is obvious that different molecules may have different rates of diffusion, and especially different ability to pass through a membrane. A *semipermeable membrane* is one which allows water molecules to pass, but not those of substances in solution. Many membranes in the body are semipermeable or approximately so.

If a container be divided into two parts by a permeable membrane and water placed on each side, there will be an interchange of water molecules between the two sides, but

the level of the fluid will remain the same because the interchange is equal in the two directions. If a solution be on one side and water on the other, the water and the soluble substance will be found to pass through the membrane at different rates in the two directions. Water molecules will pass into the solution faster than they pass out of it; the molecules of the soluble substance will not pass in either direction as readily as the water molecules. It is evident that the result of this will be to increase the volume of the solution, so that its level will be raised above that of the water. The tendency of a substance in solution to cause a more rapid osmosis of water toward it is called its **Osmotic Pressure**, and the measure of this pressure is the height to which the level of the solution will be raised before the force of gravity overcomes this tendency. As the molecules of the substance in solution also pass through the membrane there will come a time when the substance will have the same concentration on each side. Osmosis and dialysis now cease to be unequal in the two directions, for the osmotic pressure is *equal* in the two directions.

Osmotic pressure varies, then, with the *percentage strength* of the solution, but also, and this is a more determining factor in physiologic solutions, varies with the *degree of dissociability* of the substance. To give an idea of what are the values obtained, it may be stated that the following have been determined:

Osmotic pressure 0.95 per cent. NaCl	= 5088.9 mm. Hg.
Osmotic pressure 1.0 per cent. sucrose	= 494.0 mm. Hg.
Osmotic pressure 6.5 per cent. protein	= 30.0 mm. Hg.

The last is the concentration of the protein in blood-serum.

These figures express the osmotic pressure when solutions of the strengths mentioned are dialyzed against pure water through a membrane impermeable to the soluble substance. The osmotic pressure of several substances in solution is the sum of the components, and if two solutions are dialyzed against each other the result on the flow of water will depend on the algebraic sum of the osmotic pressures on the two sides.

The terms **Isotonic**, **Hypertonic**, and **Hypotonic** signify that two solutions exert the same or greater or less osmotic pressure. In physiology these terms are used to mean *osmotic pressure as compared with that of blood-serum*, which has the value of 5088.9 mm. Hg.

QUESTIONS FOR CHAPTER I

What are the characteristics which distinguish living protoplasm from dead tissue?

Name the varieties of natural stimuli; of artificial stimuli.

Is the "make" or the "break" of a galvanic current a more efficient stimulus?

Does the same relation hold with the induced current? Why?

Give the chemical formula for a monosaccharid; for a disaccharid; for a polysaccharid.

What is the chemical and the physical difference between starch and dextrin?

In what form is maltose absorbed? Are sucrose and lactose absorbed in the same form?

How are carbohydrates synthesized in the body?

What do we know about their oxidation?

What is the chemical relation between carbohydrate and fat?

Name the chief fats occurring in the body.

What do we know about the oxidation of fats?

Are lecithin and cholesterin related to fats chemically?

Is there a chemical relation between fats and proteins?

What is the important difference between amino-acids and fatty acids?

Is the amino-acid content of protein always the same?

Give the method of distinguishing between an albumin, globulin, albuminate, proteose, and peptone.

What are the end-products of amino-acid catabolism?

What is the result of amino-acid synthesis?

Why are nucleoproteins of especial importance?

Name the characteristics of an enzyme.

What is the relation between enzyme, zymogen, and kinase?

What are the main types of enzymes?

Mention the usefulness of a calorimeter.

Considering its calories, which is the most valuable food?

Why does protein produce more heat in a calorimeter than in the body?

What is the relation between osmosis, dialysis, and diffusion?

What is a semipermeable membrane?

How can osmotic pressure be measured?

Name the chief factors governing the osmotic pressure of a solution.

What would be the direction of the greatest osmotic pressure if a hypertonic and an isotonic solution were placed in a container separated by a semipermeable membrane?

CHAPTER II

MUSCLE AND NERVE

MUSCLE and nerve are highly specialized: the one for contractility, the other for conductivity. They are independently irritable.

MUSCLE

Chemistry of Muscle.—Chemically, muscle consists of water to the extent of 75 per cent. Proteins form 20 per cent., and are of two main varieties: myosin, a globulin; myogen, an albumin. A considerable amount of glycogen is also present, from 0.5 to 0.9 per cent., which, together with a certain amount of dextrose, isomaltose, and fat, form the reserve supply of fuel for muscle activity. Lactic acid, a by-product of carbohydrate metabolism, and creatin, creatinin, and the purin bases, waste products of protein metabolism, are found in variable amounts. Inorganic salts, chiefly of potassium, but also of sodium, calcium, magnesium, and iron, occur, combined with chlorin, phosphorus, and sulphur.

During contraction the muscle glycogen is converted to glucose and broken down through the form of lactic acid, with CO_2 and water as the end-products. A similar process occurs when the blood-supply ceases, and in this case results in the coagulation of the muscle proteins. This process is called **Rigor**.

Two theories as to the **Cause of Contraction** should be mentioned: (1) The chemical changes which take place result in heat production, and this heat causes the doubly refractile particles composing the dim bands of cross striated muscle and lying in the stroma of smooth muscle to imbibe water and swell. This swelling results in the characteristic thickening and shortening of the muscle-fiber. (2) The chemical change

tends to increase the surface tension of the material composing the fibrils; this results in a tendency on the part of the fibril to assume a more nearly spherical form which shortens and broadens the muscles. A muscle does not change in volume during contraction, although its dimensions are altered.

Muscle is extensible, but does not stretch in proportion to the force applied. As the elongation is increased the extensibility becomes less and less, until a point is reached where the tissues begin to tear. On cessation of stretching or other distortion, muscle, by virtue of its **elasticity**, resumes its normal shape.

Striate muscle is stimulated normally by the nerve impulse, but it will respond to the usual external stimuli. After the stimulation of a striate muscle it **contracts**, but there is a momentary delay in the appearance of the mechanical change; this is known as the latent period of muscle. When an electric stimulus is applied directly to the muscle the **latent period** amounts to about 0.005 second, using the most careful experimental technic. The usual laboratory apparatus records it as 0.01 second. The contraction produced by a single induction shock lasts about 0.1 second, but varies with the resistance offered and with the condition of the muscle. The phase of shortening takes about 0.4 second; the phase of relaxation about 0.5 second.

The contraction of a muscle-fiber is not confined to the point stimulated, but sweeps over the whole fiber as a wave, with a **velocity**, in human muscle, of about 10 meters per second.

The extent of shortening varies with the condition of the muscle, the strength of stimulus, and the weight lifted. If a muscle is chilled, the result is an increased latent period, a slower and less marked contraction, and a prolonged relaxation. Heat has the opposite result.

When a muscle is repeatedly stimulated to contract with but a brief interval between the stimuli, it is seen that though the stimuli remain of a constant strength, yet the contractions will not be all of the same height. There is at first a

slight increase in the height of the contraction, and then a gradual and steady decline. The period of increasing contractions is of considerable importance as indicating a general physiologic law, that functional activity leads to increased irritability. The period of decreasing contractions is due to diminishing irritability, and this condition is known as **fatigue**. The contraction takes place more slowly and the relaxation is much prolonged, so that eventually the muscle is in a condition of almost tonic contraction, possibly the cause of an athlete's cramps. Fatigue depends in part on the consumption of energy-producing material, but perhaps most on the accumulation of the waste products of muscular activity.

As to the strength of stimulus, we find that a given stimulus may be too weak to produce a contraction. Gradually increasing the strength, a point will be reached where a just visible contraction results; this is known as a **minimal stimulus**. If a stimulus just too weak to cause a contraction is repeated several times in succession, the irritability of the muscle will be increased and a contraction will result. Thus, by this process of *summation*, a *subminimal* stimulus will become a minimal, or in a similar manner a minimal stimulus may be effective as a *supra*-minimal stimulus. On further increasing the strength of stimulus, the extent of shortening will go on increasing up to a certain point, when the **maximal contraction** of which the muscle is capable will have been reached. Further increase of stimulus will not increase the extent of shortening. This is known as a **maximal stimulus**. If the muscle be stimulated at short intervals with the stimulus which caused a maximal contraction until it shows signs of fatigue, a further increase in the strength of the stimulus may now provoke a contraction equal to that of the fresh muscle.

If a muscle be caused to lift a **load**, any addition of weight will reduce the height to which the load is lifted, though it does not necessarily diminish the amount of work done. The **work** accomplished is the product of the load by the height to which it is raised. If the muscle contracts without lifting a

load, no external work is done. If so great a resistance is opposed to the active muscle that it cannot shorten, no work is done, the energy set free all appearing in the form of **heat** and **electricity** in both cases. When the muscle is working to best advantage, not more than one-fourth of the energy set free is converted into work. The efficiency of muscle is greatest when it contracts against a certain specific amount of resistance. The lifting power of a muscle is in proportion to its cross-section. The term **isometric contraction** is applied to a muscle contraction made when the muscle is so fixed at both ends that it cannot shorten during contraction. A record of such a contraction would show the rate at which energy is developed within the muscle. The term **isotonic contraction** is applied to a muscle contraction made under such conditions that the tension of the muscle remains constant throughout the contraction. A record of this contraction shows the rate at which motion is developed.

So far we have considered only the **twitch** or single contraction of muscle. When stimuli are so rapidly repeated that a graphic record of the contraction shows no undulations, the contraction is spoken of as a complete **tetanus**; if time is allowed for a partial relaxation between contractions, it is an incomplete tetanus. The tetanic contraction is greater in extent than that resulting from a single stimulus of the same strength. In the body it is seldom that a muscle contracts as the result of a single stimulus. Usually the contraction is more prolonged, and consists in a **tetanus**, produced by stimuli, with a frequency varying in different muscles from 40 to 100 per second. The muscles are normally maintained in a condition of slight tension known as **tone**. Tone is really a state of partial contraction, and is due to stimuli sent by the nerves from the spinal cord centers.

Plain or smooth muscle is supplied by nerves whose cells lie in the sympathetic chain, and so is out of the direct control of the will. It is called involuntary muscle, and is marked by great sluggishness in its contraction. The latent period may be as much as three or four seconds, while relax-

ation is greatly prolonged. Smooth muscle reacts much less readily to the electric current than to the other forms of stimulation. It remains in tone even when separated from the central nervous system, but this does not prove absence of nerve impulses, for all smooth muscle contains nerve-cells within its interstices. These cells may also be responsible for the tendency to rhythmical contraction and relaxation shown by smooth muscle, though both of these questions are still unsettled.

Cardiac muscle is considered by most to possess the property of inherent rhythmicity, and it is a fact that in the embryo chick the heart pulsates before the nerve-cells have grown into it. Cardiac muscle has three very characteristic properties: (1) If it reacts to a stimulus at all, it does so with the maximum contraction possible under the nutritive conditions obtaining at the time, no matter how weak or how strong the stimulus. (2) It seems to use up with each contraction all the available material upon which contraction depends, so that a more rapid rate with consequent shorter time to produce this material results in weaker contractions. (3) It does not react to a series of rapid stimuli with a tetanic contraction because it is not irritable to artificial stimuli during its phase of contraction, and stimuli during relaxation produce a lesser contraction the shorter the period of rest. Cardiac muscle will be further spoken of in the consideration of the heart-beat.

NERVE

Nerve.—The form of tissue most specialized for conduction of an impulse is nerve tissue. The nerves which when stimulated cause the muscles to contract are called motor nerves. The motor end-plates are specialized for transferring the nerve impulse to the muscle-fibers, so that a muscle will contract in response to a weaker stimulus applied to its nerve than if the stimulus is applied directly to the muscle. The normal stimulus comes, of course, from the nerve-cell, but artificial stimuli are effectual at any point in the course of the nerve.

Chemically, we know little except that the myelin sheath is composed largely of lecithin and cholesterin and a glucosid, cerebrin, which contains a nitrogenous base, fatty acids, and galactose. Oxidative processes are supposed to occur because low temperatures decrease the irritability and rate of conduction, as does deprivation of oxygen or an increase of the CO_2 in the surrounding medium. No increase in temperature nor signs of fatigue have been proved even after prolonged tetanizing stimuli.

Compression of a nerve decreases the conductivity, and the passage of a galvanic current through it may either decrease or increase conductivity. (See under Electric Phenomena.) The *nature of the nerve impulse* is still disputed; it may be the propagation of a reversible chemical change, or of an actual electric potential.

When the impulse passes along a nerve it is accompanied by a change in the electric potential. This is sufficiently intense to act as a stimulus to another nerve which lies in contact with the one which is functioning. It is readily obtained and registered by a galvanometer, and this forms the most satisfactory method of measuring the **speed** of a nerve impulse. The speed varies in the neighborhood of 30 meters a second. It is also found that from the point of artificial stimulation of a nerve an impulse passes *in both directions* along the fibers. If artificial stimuli are applied to a nerve-fiber so rapidly that the second stimulus arrives before the electric change due to the first has subsided, the fiber is not irritable to the second stimulus, and, as in cardiac muscle, the second stimulus has no effect.

ELECTRIC PHENOMENA

Electric Phenomena of Muscle and Nerve.—The passage of a galvanic current through a nerve not only modifies its irritability but also changes its conductivity. This condition is called **electrotonus** and varies at the anode and at the cathode. The increased irritability and conductivity at the cathode is called **catelectrotonus**, while the depressed condi-

tion at the anode is called **anelectrotonus**. After prolonged passage of moderate currents, and promptly with very strong currents, the anelectrotonus spreads so as to also involve the region of the cathode. Accordingly, if a motor nerve is stimulated by a galvanic current, the muscle will not contract with a strong current if the anelectrotonus is so situated as to block the passage of the impulse toward the muscle. A current is spoken of as ascending if it flows through a nerve away from the muscle, as descending if it flows toward the muscle. With *weak currents* only the stimulus at the make is sufficiently intense to cause a contraction. With *moderate currents* both the make and the break stimuli are effective. With *strong ascending currents* the stimulus at the make starts from the cathode, but the anelectrotonus between it and the muscle blocks the impulse; at the break the stimulus starts from the anode and passes to the muscle. With *strong descending currents*, at the make the stimulus starts from the cathode and passes to the muscle; at the break the stimulus, starting from the anode, is blocked by the anelectrotonus which, with strong currents, spreads well out toward the cathode. These facts form the basis of what is called **Pflüger's law**, expressed in the following table. C indicates a contraction; O, failure to contract:

PFLÜGER'S LAW

CURRENT.	Ascending.		Descending.	
	Make.	Break.	Make.	Break.
Weak.....	C	O	C	O
Medium.....	C	C	C	C
Strong.....	O	C	C	O

In order to stimulate a nerve in the intact body one electrode is usually placed over the course of the nerve, the other on some indifferent part of the body at, perhaps, some distance from the first. Under these circumstances, we cannot expect to obtain a demonstration of the law of contraction

just described, for the current, instead of being confined to and passing along the nerve, will pass obliquely through it; if the anode be over the nerve, in a sheaf of diverging lines; if the cathode be over the nerve, in converging lines. In the former case the anelectrotonic area will be narrower than the cat-electrotonic area; in the latter case the conditions will be reversed. Where the lines of force are the more concentrated, the current will be denser and its effects more pronounced. The points where the current enters and leaves the nerve form the *physiologic anodes* or *cathodes* as the case may be. With a *weak galvanic current*, therefore, a *contraction* of the muscle, which is innervated by the nerve, will be most readily excited by the stronger of the two forms of stimulus, the *making*, when the area of catelectrotonus is concentrated by placing the *cathode over the nerve*. With an intensity of current only just sufficient to give this result, no contraction can be obtained on breaking the current if the cathode is over the nerve, and no contraction occurs at the make or break when the anode is over the nerve. If we now *increase the strength of the current* little by little with the *anode over the nerve*, we shall reach a point at which there will be a *contraction at the make*. This stimulus really arises at the physiologic cathodes where the current leaves the nerve, and because the current is more diffuse, more is necessary to obtain the result than in the first case. On *further increasing the current*, the *break becomes effective* sooner with the *anode over the nerve*, for thus the current is more concentrated at the physiologic anodes where the stimulus arises. A still *further increase* in current results in a *break contraction* with the *anode over the nerve*. These facts form the basis for the **law of unipolar stimulation** which is usually summarized by the formula—

$$CCC > ACC > AOC > COC,$$

meaning that the cathodal closing contraction, anodal closing contraction, anodal opening contraction, and cathodal opening contraction have these relative magnitudes if a current

strong enough to produce all four be used. The minimal stimuli, of course, vary in the reverse direction.

When the nerves of a muscle are degenerating, the reaction, for some reason, varies from the normal, the anodal closing contraction being obtained with a weaker current than the cathodal closing contraction; this is known as the **reaction of degeneration**, and affords a means of diagnosis. Another important means of determining the condition of a muscle depends upon the fact that after the degeneration of its nerves a muscle no longer responds to the **induced current**, while its irritability to the **galvanic current** rises above the normal. Its irritability should be compared with that of the corresponding muscle on the opposite side of the body.

When a muscle or nerve is **injured** at a certain point, the electric potential at this point is lowered; the injured portion becomes negative as compared with the uninjured portion. If the injured and uninjured parts be connected by means of a conductor, —a wire, for example, —a current will flow through the conductor from the uninjured, or positive, to the injured, or negative, pole of the muscle just as it flows from the copper to the zinc of an electric battery. This is called the current of rest, or **demarcation current**. When a nerve has been divided and is dropped back into the wound, the surrounding lymph may serve to connect the injured with the uninjured portion of the nerve, a current will be set up, and the nerve may be stimulated; this must be taken into account in experimenting upon divided nerves.

Not only is an injured part of nerve or muscle electrically negative to uninjured parts, but **active** parts are negative in a similar way, as compared with resting parts. This is called the **action current** or current of action. When an uninjured portion of muscle or nerve becomes active, the difference of potential between this point and an injured point will thus be lessened, and, if the two points are connected by a conductor, the demarcation current will be, for the moment, weakened; this weakening of the demarcation current is called the **negative variation**.

If the demarcation current be led through electrodes and wires to a galvanometer, the instrument will be deflected a certain distance from zero and will remain at that deflection. The *negative variation* shows as a *monophasic current*, a wave-like diminution of the deflection followed by a return to the former position as the activity subsides.

When *both electrodes are placed upon an uninjured* portion of muscle or nerve no current will pass. If a stimulus be applied outside of the region between the electrodes, the activity passing through the tissue reaches first one electrode and then the other. This results in the flow through the galvanometer of a *diphasic current*. As the negativity accompanying the activity approaches one electrode, current flows through the instrument toward this side; as it reaches the middle region, current flows equally to both sides and there is no deflection; as it approaches the other electrode, current flows through the instrument toward this side producing a deflection in an opposite direction. Starting from zero, the deflection is first to one side, then passes zero to the other side, and returns again to zero. Cardiac muscle seems to form an exception in this respect, the action current being very complicated.

QUESTIONS FOR CHAPTER II

Is the contraction of muscle dependent on catabolic or anabolic changes?

What is meant by the conductivity of muscle?

In order to produce complete tetanus, why is the frequency of stimulation that is required less in the case of a fatigued than in the case of a fresh muscle?

If an isolated muscle has been fatigued by continued stimulation, why does washing out its vessels with normal salt solution tend toward the recovery of its irritability?

Do the irritability and conductivity of a nerve-fiber always vary in the same direction?

What is the effect of treating a muscle with the extract made from a fatigued muscle?

If on passing a constant current through a muscle the intensity of the current be suddenly raised, at which electrode will contraction begin?

On stimulating a nerve trunk in the intact body with the constant current, by the application of which electrode may we expect to succeed with the weakest current?

If in this respect the response is abnormal, what are we to conclude?

If a muscle fails to respond to the induced current, but is hyper-irritable to the constant current, what must we conclude?

If a nerve has been divided, how can we determine when its regeneration is complete?

What causes an extremity to "go to sleep"?

What are the distinguishing features of the contractile properties of the three types of muscle?

Describe the phenomenon of summation of stimuli.

What are the points of similarity between the contraction of a muscle and rigor?

How can it be proved that a muscle produces electricity?

What are the chief differences between striate muscle, smooth muscle, and cardiac muscle?

CHAPTER III

THE NERVOUS SYSTEM

THE NERVE-CELL

EVERY nerve-fiber is an outgrowth from, or a process of, a nerve-cell. A nerve-cell usually has several processes; one, the axis-cylinder process, or **axon**, becomes a nerve-fiber and is the efferent path for the cell. The others branch freely and are usually very much shorter than the axon; they are called **dendrites**, and provide the afferent or receptive path. A nerve-cell with its processes constitutes a **neuron**. Each process is dependent for its existence upon connection with the parent nerve-cell; if a nerve-fiber be divided, the portion that is cut off from the cell invariably dies; regeneration can only occur through the growth of that portion of the axon which remains in connection with the nerve-cell. Division of the axon produces secondary effects on the cell itself; the cell body shows signs of degeneration, which, if regeneration of the axon does not occur, usually becomes complete. If conditions are favorable to regeneration and the axon grows out to, and makes physiologic connection with the muscle, the cell recovers.

The nerve-cells of the posterior spinal root ganglia are originally bipolar; they give off but two processes. Later, these two processes unite for a short distance, rendering the cell body unipolar. Each process becomes a medullated nerve-fiber: one, distributed to peripheral structures, functions as a dendrite; the other enters the spinal cord and is undoubtedly an axon. These cells suffer less from a division of their processes than is the case with the cells of the spinal cord.

Nerve-cells dispatch impulses through their axons; they are excited by stimulation of their dendrites. A nerve-fiber, if stimulated midway in its course, transmits impulses in both directions, but a visible result occurs at one end only. In the case of an efferent nerve-fiber, —a motor fiber, for example, — the only appreciable result is muscular contraction, though by means of a galvanometer an action current may be shown to travel along the nerve in both directions; no change appears to be caused in the motor cell by the entrance of the impulse. If the dendritic process be stimulated, as can be done in the case of the cells of the spinal root ganglia, the visible result is that of the central discharge of the impulse. No effect will be produced at the periphery, though here again a galvanometer will show the passage of an impulse. The result of a nerve impulse is thus seen to depend upon the endings of the axon process, which are always specialized for a certain function. These endings are susceptible to fatigue, though, as has been stated, the fibers themselves are not.

When an impulse travels along a nerve-fiber, it spreads into any branches that are given off; the result of this is that if one branch of a motor nerve-fiber be stimulated near its muscular termination, the impulse which passes up the fiber toward the spinal cord will spread into any branch that happens to be given off at a higher level, and traveling down this, may cause the contraction of another muscle-fiber. This is called a **pseudoreflex**.

Contrary to what obtains in the nerve-fiber, it is believed that summation of stimuli is possible in the nerve-cell, *i. e.*, that subminimal stimuli if repeated may become effective.

THE SPINAL CORD

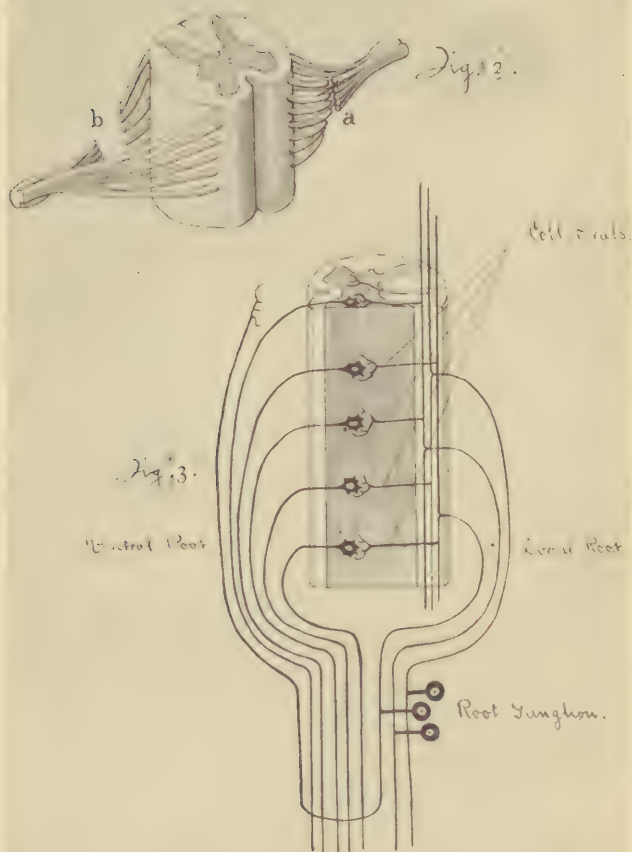
In the grouping of its nerve-cells and in its relation to the tissues of the different parts of the body, the spinal cord shows a segmental arrangement, though each segment is intimately connected with the rest of the central nervous system.

From each segment arises a pair of spinal nerves, through

which relations with a particular segment of the body are established; there is, however, an overlapping of the innervation of a particular body segment, so that a given muscle receives nerve-fibers from two or three segments of the cord; this is especially the case with the muscles of the limbs. In consequence of this arrangement, a lesion which is strictly confined to one segment of the cord never deprives any one muscle of its nerve supply.

Each spinal nerve is connected with the cord by two roots, a ventral, or anterior, and a dorsal, or posterior, root, and each of these, where it joins the cord, is divided into several small rootlets, which are shown in Fig 2. If the **anterior nerve-root** be divided, as at *a*, degeneration of the peripheral portion of the root occurs, and many nerve-fibers will be found to degenerate in the common nerve-trunk as far as its terminations in the muscles and sympathetic system. The fibers of the anterior root arise from cells which are situated in the gray matter of the cord, at the level of each fiber's exit. The portion of the anterior root which remains in continuity with the cord does not degenerate at once, for it has not been separated from its parent cell, as is the case with the portion peripheral to the lesion.

Division of the **posterior spinal** nerve-root at a point between the root ganglia and the cord, as at *b*, Fig. 2, leads to degeneration of the rootlets which are left in connection with the cord, and degeneration of the posterior root-fibers may be traced within the cord, upward as far as the spinal bulb, downward for a short distance only. No degeneration occurs peripheral to the lesion, for the posterior root-fibers are the axons of posterior root-ganglion cells, and only that part of a fiber which is cut off from its parent ganglion cell is destroyed. If the **posterior root-ganglion** is removed or crushed, the resulting degeneration destroys not only the nerve-fibers which have grown from the ganglion into the spinal cord, but those also which are distributed to the periphery through the spinal nerve-trunk. Division of the **spinal nerve-trunk** at a point peripheral to the root-ganglion causes degeneration,



Figs. 2 and 3.—Fig. 2. Anterior and posterior nerve-roots. Fig. 3. Cell connections of fibers of nerve-roots.

peripheral to the lesion, of all its fibers; central to the lesion, of none.

Fig. 3 shows the cell connection of the fibers of both roots. It will be noticed that the peripheral process of one posterior root-ganglion cell is represented as turning aside into the anterior nerve-root, instead of accompanying its fellows down the spinal nerve-trunk. The fibers which follow this course are distributed to the membranes of the cord, etc.

If the nerve-roots be divided as shown in Fig. 4, and the peripheral cut end of the **anterior root** be stimulated at *a*, there will result a contraction of the muscle *M*, to which some of the fibers of this nerve are distributed. This result will not be prevented by previous destruction of the posterior root-ganglion and degeneration of the posterior root-fibers. The anterior root contains motor nerve-fibers which are the axons of spinal cells. Stimulation of the central cut end of the anterior nerve-root, at *b*, produces no visible effect, for the resulting nerve impulses are evidently unable to spread to other neurons within the cord, though they probably reach the motor cells whose axons are stimulated.

On stimulation of the central cut end of the **posterior nerve-root**, at *c*, there may occur a reflex contraction of the muscle *M'*, and, if the spinal cord be intact and connected with the brain, sensation. The nerve impulses excited in the posterior root-fibers enter the cord and are transmitted by the ascending branches of these fibers toward the brain, and by their collateral branches (Fig. 3) to the motor cells of the gray matter. The motor cells are thus stimulated, and dispatch impulses through the anterior root to the structures which they innervate. Such a motor impulse is called a **reflex**. Stimulation of the peripheral cut end of the posterior root, at *d*, produces, as far as can be determined, no result.

The fibers of the anterior nerve-roots are **efferent**; they transmit impulses from the cord to the periphery. These fibers are more irritable the nearer to the cord the stimulus is applied. The fibers of the posterior nerve-roots are **afferent**; they transmit impulses from the periphery to the spinal cord.

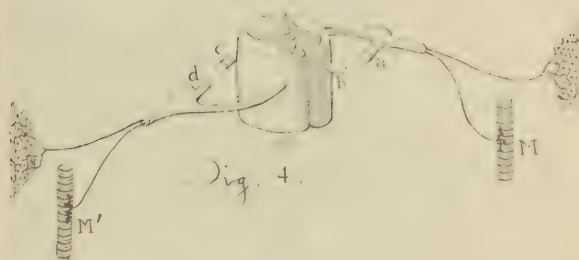
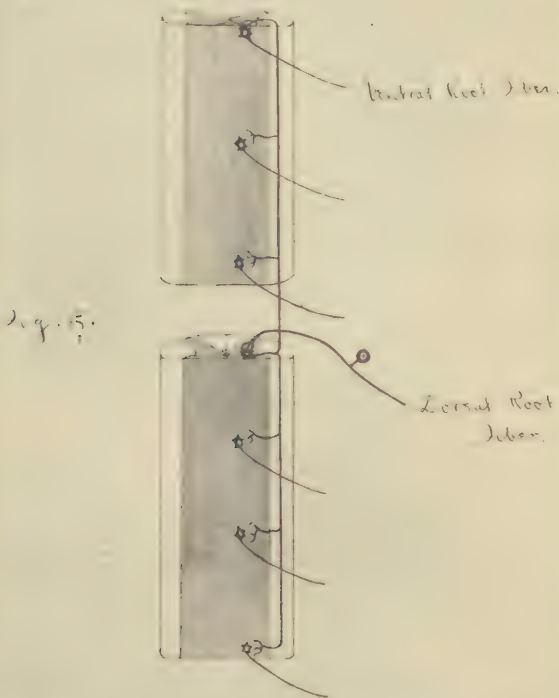


Fig. 4.



Figs. 4 and 5.—Fig. 4. Distribution of nerve-fibers of the roots. Fig. 5. Representation of a reflex involving three neurons.

An afferent neuron and an efferent neuron together constitute the simplest form of **reflex arc**. A more elaborate form of reflex arc, including three neurons, is shown in Fig. 5. As will be seen, this form allows a more widespread reflex, through the stimulation of a greater number of motor cells. The axons of the central, or mediate, cells do not leave the central nervous system, but ascend and descend the cord, thus bringing different levels into communication with one another. Some cross the median line and afford a basis for crossed reflexes; neurons of this class are called **commissural**.

The time for a simple reflex has been found in the frog to be about 0.015 second, and the wink reflex in man has been estimated at about 0.04 second.

In some of the lower animals, for instance, the fish, reflexes may be carried on by one segment of the cord after it has been isolated from the rest. As a general rule, the reflex irritability of the spinal cord is increased by excluding the impulses which normally descend from the brain. In the **spinal animal**—that is, one whose cord, or the greater portion of it, has been separated from the brain—it is easier to predict the kind of reflex that will be evoked by a given stimulus. If a spinal dog be held in a vertical position, the stretching of the skin on the pendent legs will give rise to a reflex raising of these. A minimal stimulus applied to the skin will provoke reflex contraction of muscles on the same side of the body; if the intensity of the stimulus be raised, the reflex may spread to the opposite side also. Reflexes spread tailward more readily than headward; it is more difficult to cause reflex movement of the foreleg by stimulation of the skin of the hinder part of the body than to cause movements of the hind limb by stimulating anteriorly. It is impossible to cause reflex simultaneous contraction of antagonistic muscles; if the flexors of a limb contract, the extensors relax, and vice versa. The relaxation is due to an inhibition of the motor cells which control the **antagonistic muscles**.

The skeletal muscles possess a **tone** which is of reflex origin; they are kept in a state of slight tonic contraction by weak

motor impulses which continually reach them from the spinal cord cells, the activity of these cells resulting from the constant arrival of afferent nerve impulses from the periphery. The motor nerve-cells of the cord discharge impulses rhythmically at a rate varying in different cells from 40 to 100 per second. If the motor cells be inhibited by impulses coming to them from the brain, or from a contracting antagonistic muscle through afferent nerves, their activity is lessened and the muscles which they govern are allowed to relax; their tone decreases. The division of its nerve supply puts an end to the tone of a muscle, as may be readily understood. During sleep muscular tone disappears.

When a muscle loses its tone, it also loses what is known as **myotatic irritability**, which consists in the power of a muscle, when stretched, to respond to a mechanical stimulus. The **knee-jerk** which is evoked by tapping the patellar tendon when the extensor muscles are put on the stretch depends on myotatic irritability. Whether this contraction is a true reflex, *i. e.*, the efferent result of an afferent nerve impulse, or is contraction in response to the mechanical stimulation of the muscle by tapping, is still a disputed point. The latest evidence points more strongly toward it being a true reflex, but at any rate it is intimately dependent on the existence of reflex muscular tone; an injury to the reflex arc, upon the integrity of which muscular tone depends, abolishes the knee-jerk. This is the case in *tabes dorsalis*, in which the posterior nerve-roots are affected. The knee-jerk also disappears when injury is done to the lumbar region of the cord, wherein lie the motor cells concerned. On the other hand, a lesion situated above this region may, by preventing cerebral inhibition from reaching these cells, render them more irritable than in the normal condition, and result in exaggeration of the knee-jerk. The extent or absence of myotatic irritability is, consequently, a symptom of diagnostic import.

The **condition of the reflexes** innervated by different portions of the spinal cord is of great assistance in determining the position of a lesion; as instances, the following may be

mentioned: the *scapular reflex*, controlled by the fifth cervical to the first thoracic segments; *palmar reflex*, seventh cervical to first thoracic; *epigastric reflex*, fourth to seventh thoracic; *abdominal reflex*, seventh to eleventh thoracic; *cremasteric reflex*, first to third lumbar; *knee-jerk*, second to fourth lumbar; *gluteal reflex*, fourth and fifth lumbar; *plantar reflex*, first and second sacral; *Achilles tendon reflex*, third to fifth sacral. These centers become hyperirritable when, by injury to the pyramidal tracts, the control exercised by the brain is eliminated, though, in man, complete division of the cord is followed by depression of the centers situated below the lesion. The reflexes are abolished by degeneration of the spinal centers which control them. The muscles concerned show the reaction of degeneration.

AFFERENT CONNECTIONS OF SPINAL NERVES

As was stated above, the **central axons** of the posterior spinal root-ganglion cells, on entering the cord, divide into ascending and descending branches. The former are the longer, but vary in length. Both branches finally end in the gray matter, some ascending as far as the medulla; both give off **collaterals** (Fig. 3), which also end in the gray matter. The course of these fibers is in the posterior, or dorsal, columns of white matter, each of which is subdivided into a **dorso-median** and a **dorsolateral tract** (Figs. 6, 7). The fibers ascend at first in the dorsolateral tract, but the longer fibers from the lumbar nerves which pass up to the medulla cross over into the dorsomedian tract, and thus reach the dorsomedian nucleus, or **nucleus gracilis** (Fig. 6) of the medulla, where they end. The dorsolateral tract, when it reaches the medulla, consists chiefly of fibers which carry impulses from the upper extremities; these fibers end in the dorsolateral nucleus, or **nucleus cuneatus** (Fig. 6). These two nuclei serve as cell stations for the forwarding of impulses to the cerebellum and to the cerebrum, in response to impulses received from the periphery. They contain nerve-cells whose

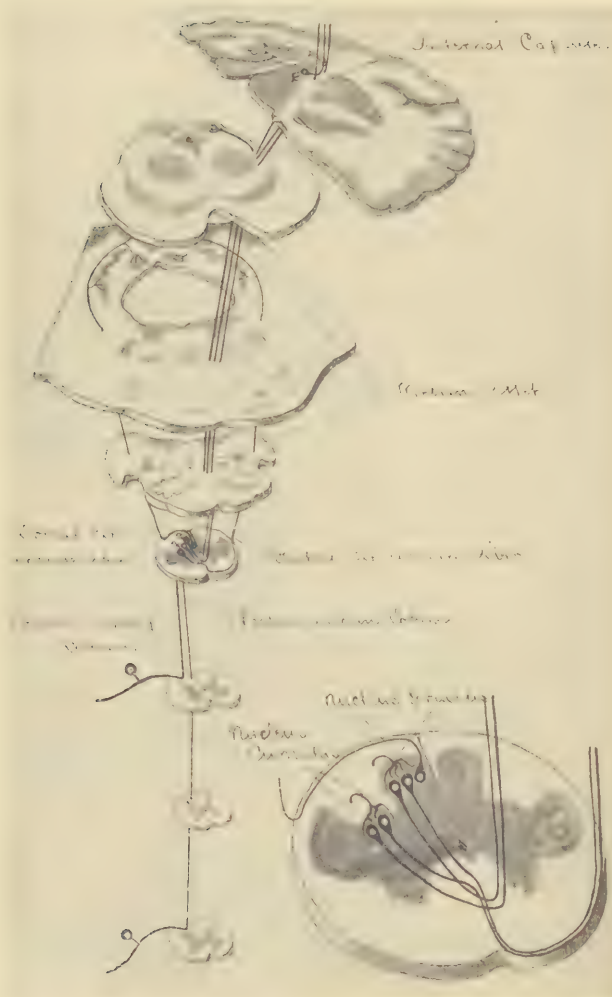


Fig. 6. Serial sections showing the course and connections of the posterior root-fibers.

axons follow several different paths; some, the internal arcuate fibers, curve ventralward, cross the median line, and ascend in the fillet, or lemniscus, on the opposite side, toward the cerebrum (Fig. 6). Probably only the minority of these reach the cortex; many of them end at lower levels in, for instance, the optic thalamus and corpora quadrigemina. The optic thalamus seems to afford another cell station on the way to the cerebral cortex. In the internal capsule the ascending fibers are found in the posterior portion of the dorsal limb.

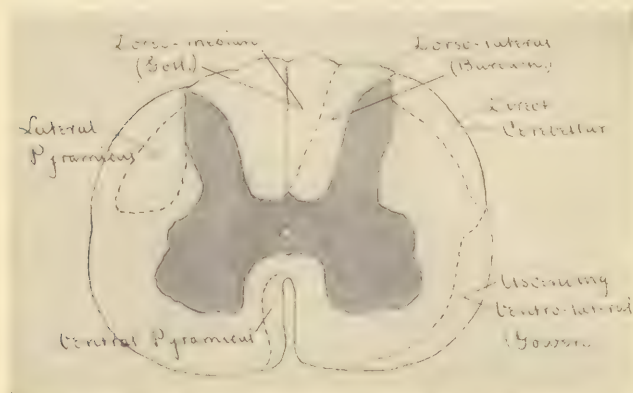


Fig. 7.—The ascending and descending tracts of the spinal cord in cross-section.

The dorsal nuclei are connected with the cerebellum, through the restiform body, by two sets of fibers; one set, arising from the cells of these nuclei, passes directly into the restiform body on the same side; another set, the external arcuate fibers, follows the same course as the internal arcuates until, the median line having been crossed, they reach the surface, and, passing in front of the pyramid, enter the restiform body, and so, the cerebellum. The fibers which thus reach the cerebellum carry impulses to the roof nuclei and cortex of the inferior vermis.

It is highly probable that impulses which are concerned in **muscle-sense** ascend the cord and reach the cerebellum and cerebrum over the paths just described; there is some evidence that the impulses concerned in *tactile sensibility*, *pressure sense*, also follow this course.

If the posterior nerve-roots be divided, the degeneration of fibers within the cord is confined to those in the dorsal columns. Division of the cord itself is followed by the degeneration of not only the dorsal column fibers which have entered below the point of lesion, but of fibers situated in other tracts. Fig. 5 shows central cells whose axons ascend and descend the cord for short distances, in that part of the white matter which is adjacent to the gray. Many of these will be divided in making a transverse section of the cord, and degeneration will occur in that portion of the fiber which is separated from its parent cell; in those which have grown from below upward degeneration will occur above the lesion; those which have grown downward will degenerate below the lesion. In addition to these, fibers of much greater length will be found to degenerate both above and below the point of section.

One distinctly marked ascending tract, whose fibers degenerate above the point of section, is the **direct cerebellar tract** (Figs. 7, 8). The fibers which constitute this tract originate from a group of cells which persists throughout the thoracic cord, and is known as the *column of Clarke*, or the vesicular cylinder. The group lies at the base of the posterior horn of gray matter and toward its median border. In the neighborhood of these cells many of the dorsal column collaterals end, and thus bring the group under the influence of the afferent impulses which enter through the posterior roots. The direct cerebellar tract ascends the cord without undergoing decussation and enters the cerebellum through the restiform body, its fibers ending chiefly in the cortex of the vermis, partly on the same, partly on the opposite side. What afferent impulses are carried by this tract is uncertain. It must be remembered that impulses which reach the cerebel-



Fig. 8.— Serial sections showing the course and connections of the direct cerebellar tract. (The upper section is disproportionately reduced.)

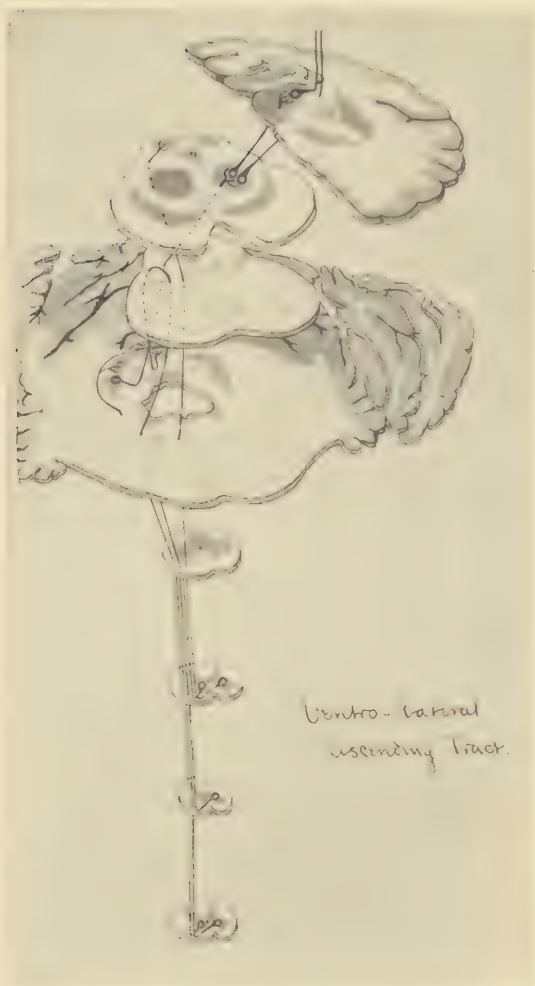


Fig. 9.—Serial sections showing the course and connections of the antero-lateral tract. (Upper section disproportionately reduced.)

lum may cause the dispatch of cerebellar impulses to the cerebrum, for the two are intimately connected through the superior cerebellar peduncle, or brachium conjunctivum (Fig. 8).

Another ascending tract is that of Gowers, or the **antero-lateral ascending tract** (Figs. 7, 9). Its fibers originate from cells situated in the gray matter, on the same and on the opposite side of the cord; they pass for the most part into the cerebellum, some ascending as far as the level of the inferior corpus quadrigeminum, and then curving downward into the vermis; others entering the cerebellum through the restiform body. Mixed with these fibers are some which do not enter the cerebellum, but end in the corpora quadrigemina and optic thalamus. This tract appears to convey impulses concerned in **temperature sensations** and **pain**. Destruction of the ventrolateral portion of the spinal cord on one side leads to loss of the perception of painful stimuli, of heat and cold, when these are applied to the skin on the opposite side of the body below the lesion.

AFFERENT CONNECTIONS OF CRANIAL NERVES

Of the **cranial nerves**, the first, second, fifth, both divisions of the eighth, the ninth, and tenth contain afferent nerve-fibers. In the case of the fifth, eighth, ninth, and tenth these afferent fibers behave much as do the afferent fibers which enter the cord; on entering the medulla they divide into ascending and descending branches, the latter being, however, the longer; from these collateral branches are given off.

The afferent fibers of the **tenth cranial nerve**, vagus or pneumogastric, have a wide distribution and carry impulses from the heart, lungs, pharynx, larynx, trachea, esophagus, stomach, intestines, liver, pancreas, and spleen. These fibers, on entering the medulla, divide into short ascending branches which end in the **nucleus alæ cinereæ**, and long descending branches which form the **tractus solitarius**, or solitary bundle. These give off many collaterals which end amongst cells that

are scattered along this tract and form the nucleus of the solitary bundle. The axons of the cells of these two nuclei follow a course similar to that of the internal arcuate fibers which originate from the cells of the gracile and cuneate nuclei.

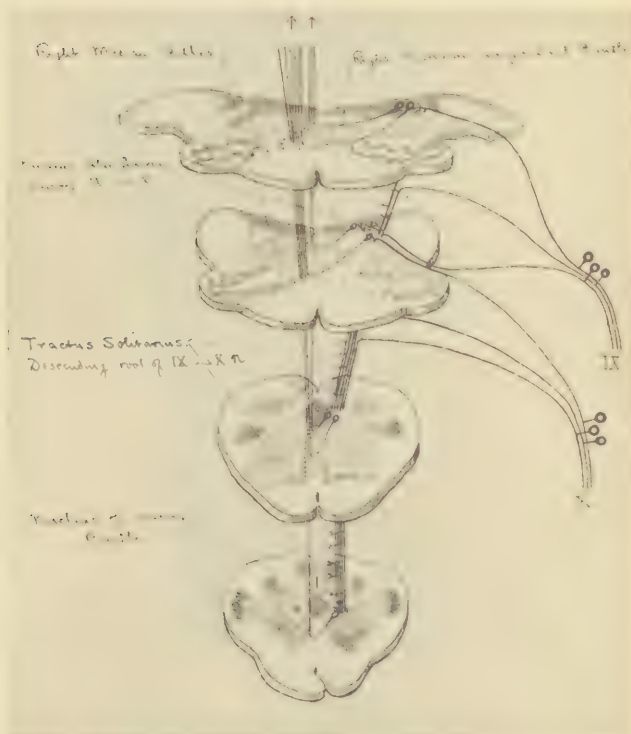


Fig. 10.—The afferent fibers of the ninth and tenth cranial nerves.

They curve through the reticular formation to the median line, cross it, and ascend in the opposite fillet; some fibers, however, enter the posterior longitudinal bundle and ascend in this toward the brain (Fig. 10). The further course of the

fibers which enter the fillet is the same as that already described (Fig. 6). These fibers, before they decussate, give off collaterals which end in the reticular formation, and may be supposed to influence the cells of the cardio-inhibitory, respiratory, and vasoconstrictor centers which are situated in this neighborhood.

The **ninth cranial nerve**, or glossopharyngeal, contains afferent fibers, which carry impulses from the tongue, pharynx, Eustachian tube, etc. Its central connections are much the same as those of the pneumogastric (Fig. 10).

The cochlear, or **auditory division of the eighth cranial nerve**, consists of afferent fibers which are distributed to the cochlea, and carry auditory impulses. These fibers are the axons of the bipolar cells of the **spiral ganglion**; in the medulla they end in two nuclei, the **ventral** and **dorsal cochlear nuclei**. The axons from the cells which form these nuclei pass through the trapezium and striæ acusticæ, as shown in Fig. 11, to the *superior olive* on the opposite side; some, however, end in the superior olive on the same side. Many of the fibers end in the olive; others pass through it and ascend, with the axons of olivary cells, in the *lateral fillet*. The fibers of the lateral fillet end on the same side in the inferior corpus quadrigeminum, in the medial geniculate body, and a few in the superior corpus quadrigeminum; and on the opposite side, in the inferior corpus quadrigeminum. From the geniculate body impulses are forwarded to the cerebrum; the corpora quadrigemina probably act as centers through which sounds may bring about reflex movements of the head and eyes. The auditory impulses pass chiefly to the opposite side of the brain, but it will be seen from the diagram (Fig. 11) that there are several means of communication with the same side of the brain.

The **vestibular division of the eighth cranial nerve** consists of afferent fibers which arise from the vestibular ganglion cells. The peripheral processes of these bipolar cells end in the vestibule and semicircular canals. This nerve carries afferent impulses, by means of which we are informed of movements of the head or of the body as a whole, and which

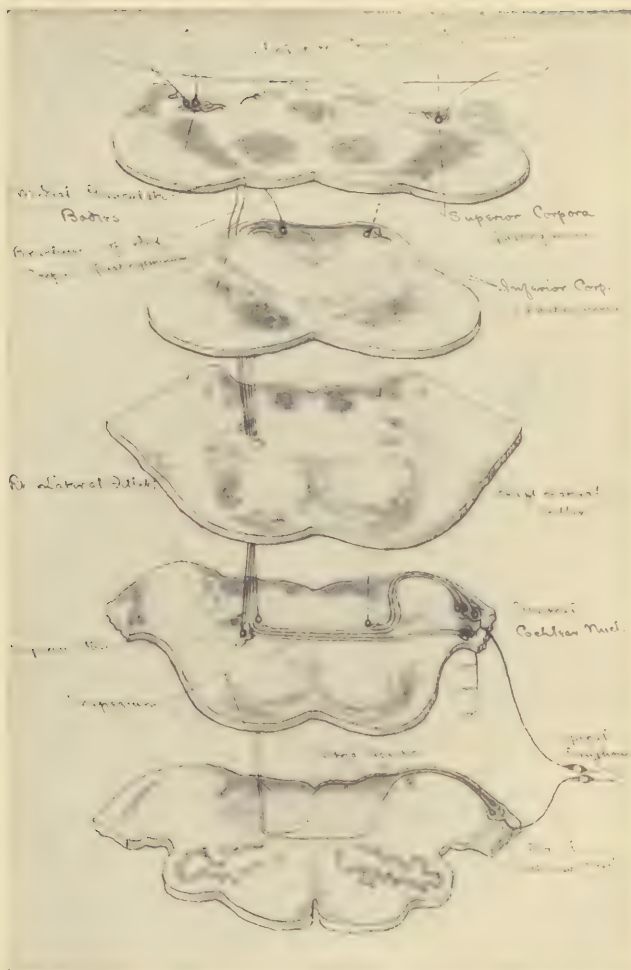


Fig. 11.—The cochlear nerve.

assist in the reflex and voluntary maintenance of **equilibrium**. On entering the medulla at the lower border of the pons,

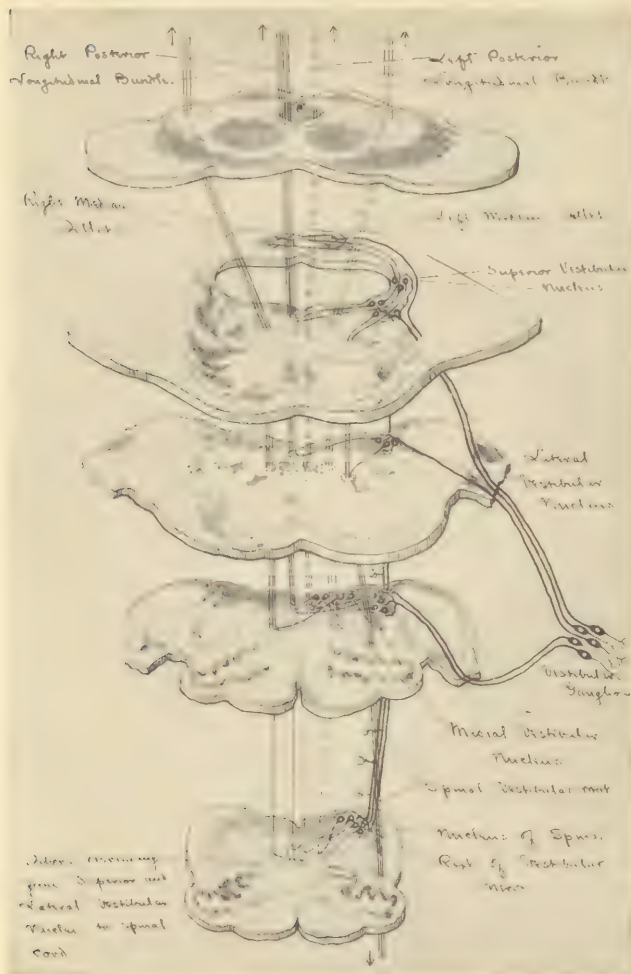


Fig. 12.—The vestibular nerve.

they end, for the most part, in four nuclei—namely, the superior, lateral and medial vestibular nuclei, and the

nucleus of the descending, or spinal, vestibular root. Some fibers pass directly into the cerebellum. The axons of the vestibular nuclear cells follow several different routes; axons from each nucleus enter, and ascend in the median fillet and posterior longitudinal bundle, mainly on the opposite side; from the lateral and superior nuclei fibers also pass into the cerebellum, while others descend the cord; both these sets probably play a part in reflex equilibrium (Fig. 12).

The **fifth cranial nerve**, trigeminus or trifacial, contains afferent fibers which carry impulses from the skin of the face, from the conjunctiva, and from the mucous membranes of the nose and mouth. Some of the fibers distributed to the tongue may carry impulses which result in sensations of taste. The afferent fibers of the trigeminus originate from cells situated in the **Gasserian ganglion**. On entering the pons they divide into very short ascending branches which end in the **chief trigeminal nucleus**, and very long descending branches, the spinal root, whose collaterals end amongst the cells of the **substantia gelatinosa** which forms the nucleus of the spinal root. The axons which arise in these nuclei give off collaterals in the reticular formation, and probably ascend in the median fillet on the opposite side of the median line (Fig. 13).

The **second cranial**, or optic, nerve differs entirely in its method of development from the other afferent nerves that we have considered: it may, however, be described with them. It consists chiefly of afferent fibers which are the axons of **retinal ganglion cells**. Light which falls upon the retina does not stimulate these cells directly, but takes effect upon the rods and cones of the outer layer. Between the rod and cone cells and the ganglion cells mediate the bipolar neurons of the retina. The axons of the retinal ganglion cells enter the optic nerve and pass along it to the optic chiasma; here the fibers from the nasal half of the retina, and some of those which originate from the cells in the macula lutea, decussate, and enter the opposite optic tract; the fibers from the temporal half of the retina do not cross, but proceed through the optic tract on the same side toward the brain. The optic

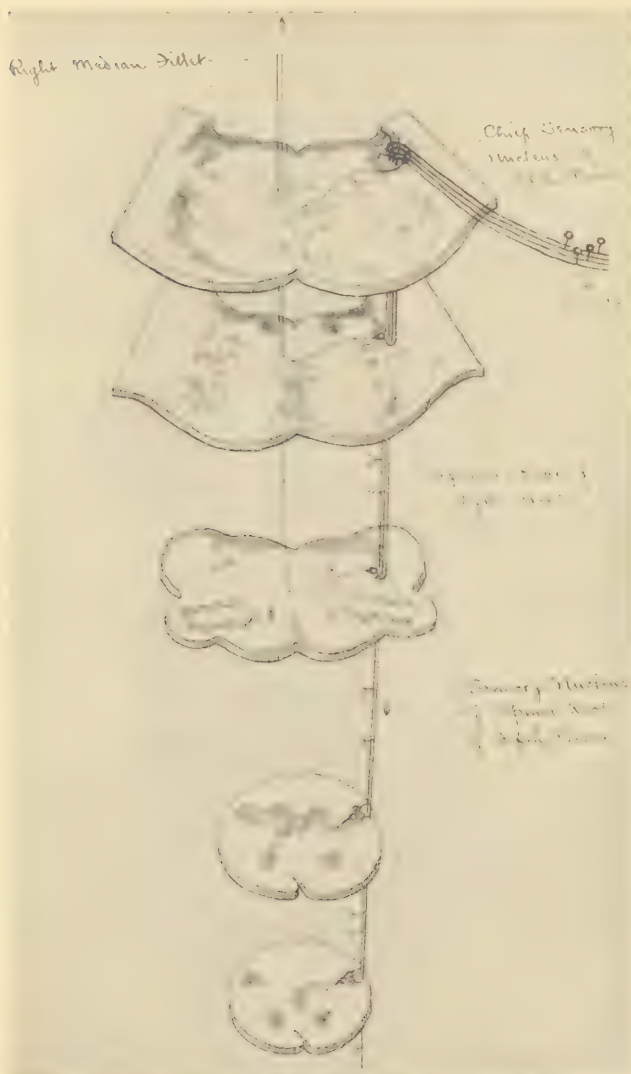


Fig. 13.—The afferent fibers of the fifth cranial nerve.

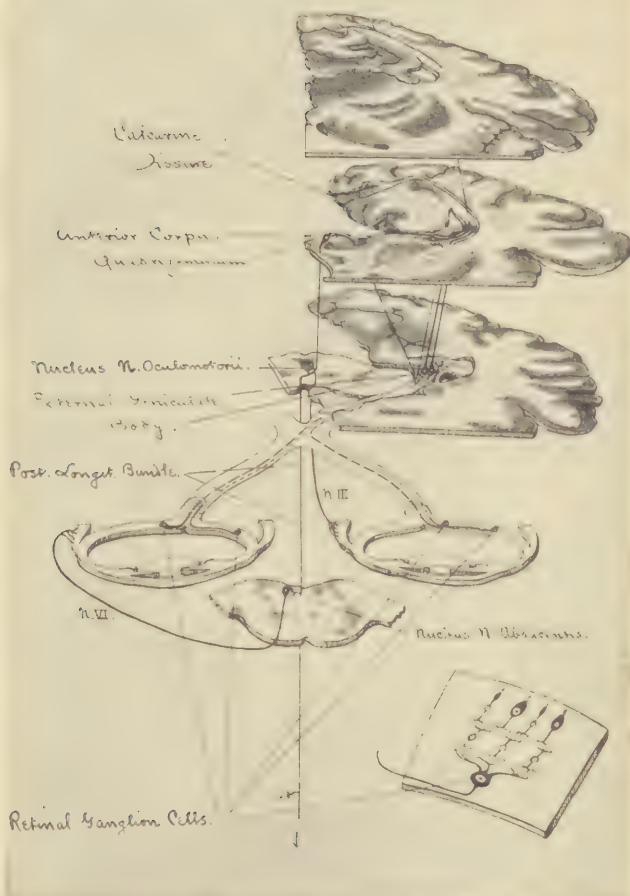


Fig. 14.—The optic nerve.

tract, then, contains fibers from the temporal half of the homonymous retina, fibers from the maculæ luteæ of both eyes, and fibers from the nasal half of the contralateral retina.

These fibers reach and end in the **external geniculate body**, the **pulvinar**, and the **anterior corpus quadrigeminum**. Axons originating from the cells of these bodies transmit impulses through the optic radiation to the occipital cortex, which constitutes the **visual area** of the brain. The **anterior corpus quadrigeminum** forms a center through which **visual reflexes** are probably inaugurated; fibers originate here which decussate and descend through the posterior longitudinal bundle into the spinal cord, giving off, on their way, collaterals which terminate in the motor nuclei of the nerves which innervate the muscles of the eye. They very probably also bring about reflex turning of the head in response to visual stimuli (Fig. 14).

The **first cranial**, or olfactory, nerve consists of the axons of cells situated in the olfactory mucous membrane of the nose; the dendrites of these cells reach the surface; their axons pass through the cribriform plate of the ethmoid bone and enter the **olfactory bulb**. The axons end here in the olfactory glomeruli, in contact with the dendrites of the mitral cells, whose axons form the second link in the chain which transmits olfactory impulses toward the brain. The mitral cell axons run in two directions; one set enters the anterior commissure, and, passing through it, reaches, on the one hand, the **opposite olfactory bulb**, on the other, the **opposite hippocampus**. Of the other set, the majority of fibers pass through the lateral olfactory gyrus to the **uncus**, where they end. The fibers of the medial root end in the **trigonum**, where they make cell connections which bring them into communication with other parts of the olfactory area. From the cells of the uncus, in contact with which the fibers of the lateral root end, axons pass to the hippocampus. The hippocampal neurons, in turn, make, through the fornix, manifold connections, some of which are shown in Fig. 15. Some of the fibers end in the nucleus habenulæ, whence neurons descend through Meynert's retroflexed bundle; others end in the corpus mammillare, and make connections with neurons whose axons divide into two branches, one ascending to the anterior nucleus of the optic thalamus, the other descending.

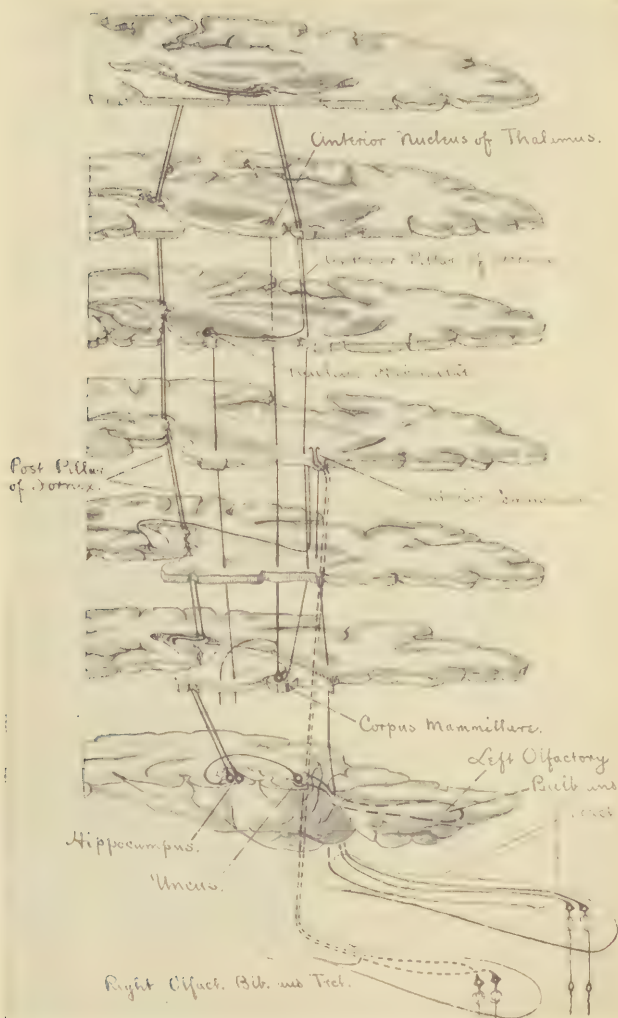


Fig. 15.—Olfactory connections.

SENSORY CORTICAL AREAS

Certain areas of the cortex cerebri are closely associated

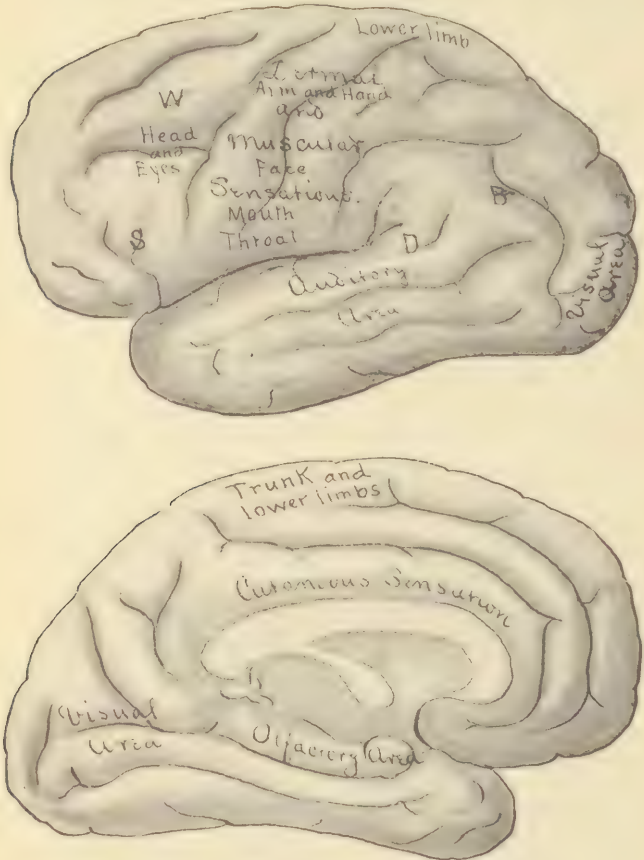


Fig. 16.—Sensory areas of the cortex cerebri.

with sensation, and it is to these areas that impulses provocative of sensation are carried. Destruction of the left occipital

lobe leads to blindness of the left half of each retina; destruction of the right occipital lobe causes blindness of the right half of each retina. The cortical area lying on either side of the calcarine fissure is probably concerned in reception of impulses from the macula lutea, or area of most distant vision, of each eye. Fig. 16 shows the visual and other sensory areas of the cortex, those for cutaneous sensibility being, however, of doubtful location.

DESCENDING TRACTS OF THE SPINAL CORD

Having considered the channels through which afferent nerve impulses are carried from the periphery to the brain, there remain for description the connections between higher centers and the peripheral efferent neurons. After transverse sections of the spinal cord degeneration of certain nerve-fibers occurs below the lesion; these degenerated fibers are, of course, the processes of cells which are situated at various levels above the lesion. There are many cells in the gray matter of the cord whose axons enter the white columns, and ascend or descend, for comparatively short distances, to end in the gray matter at different levels; on their way through the white matter they give off collaterals which also enter and end in the gray matter (Fig. 5).

In addition to these there are fibers which descend into the cord from higher levels. Two such tracts have already been mentioned—namely, the fibers which descend from the **vestibular nuclei** (Fig. 12), and those which descend in the posterior longitudinal bundle from the superior **corpus quadrigeminum** (Fig. 14). Both these sets of fibers descend through the ventrolateral columns of the cord and give off collaterals to the gray matter. Fibers also descend, in all probability, from the **cerebellum**, though these may be interrupted by cell stations in the inferior olives or in the pons. There is no doubt that the cerebellum, either directly or indirectly, exerts an influence over the motor neurons of the cord, for its removal results in marked interference with the coördination of

movements and the maintenance of equilibrium. Another set of fibers descends from the **red nucleus** (Fig. 8) into the

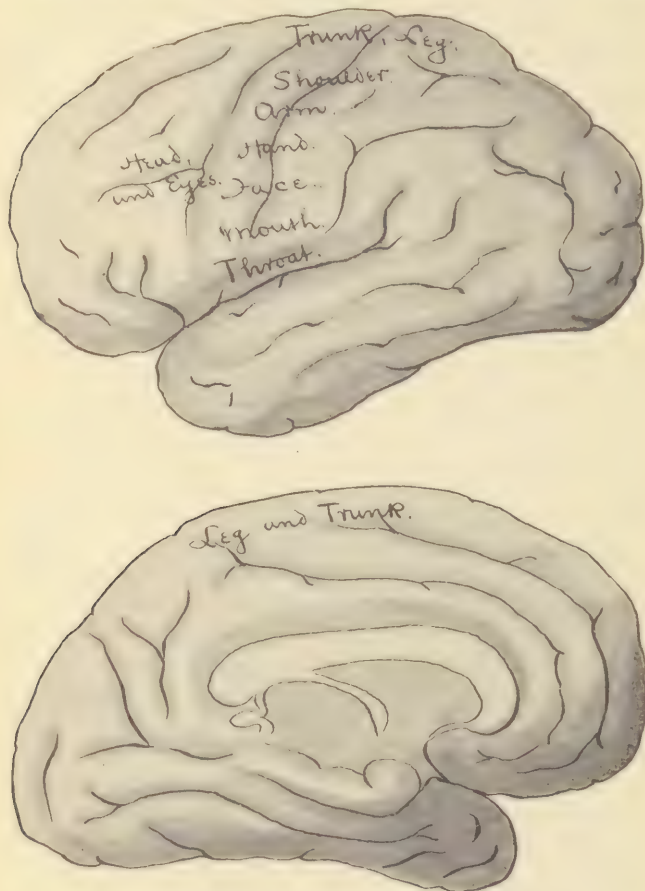


Fig. 17.—Motor areas of the cortex cerebri.

opposite half of the spinal cord, and is found just medial to the direct cerebellar tract. Two descending tracts, with the

course and function of which we are better acquainted, are the direct and crossed pyramidal tracts. It is perhaps better to call them the **ventral** and **lateral pyramidal tracts** (Fig. 7). They originate chiefly from cells which are situated in what are known as the **motor areas of the cortex**.

It has been found that the stimulation of certain areas of the cortex cerebri results in the contraction of certain groups of muscles. Fig. 17 shows the distribution of these areas.

In these areas are large pyramidal cells—so called on account of their shape—whose axons pass through the corona radiata to the **internal capsule**, of which they form the knee and anterior two-thirds of the posterior limb (Fig. 18). The arrangement of the pyramidal fibers in the internal capsule shows a certain correspondence to that of the motor areas from which they originate; most anteriorly are situated the fibers from the motor area for the eyes, then come those for the head, and these are followed in order by those for the tongue and mouth, shoulder, elbow, wrist, fingers, trunk, hip, knee, toes. The arrangement of these fibers in definite groups according to their origin persists throughout their course, though even in the internal capsule there is some admixture.

The pyramidal fibers pass down through the middle portion of the crusta of the cerebral peduncle, and through the ventral portion of the pons, into the medulla, where they form the pyramid from which their name is derived. At the lower end of the medulla the majority of the fibers cross, in the **pyramidal decussation**, into the **lateral pyramidal tract** on the opposite side, and, descending the cord, end at successive levels in the gray matter near Clarke's column. The stimulation of the motor cells of the anterior horn must, therefore, entail the mediation of an intervening neuron, which perhaps stimulates several motor cells. Not all the pyramidal fibers decussate in the medulla; a few pass into the lateral pyramidal tract of the same side, some descend in the homonymous **ventral pyramidal tract**. The fibers of the ventral pyramidal tract decussate at various levels of the cord and end in the gray matter of the opposite half. The fibers which without cross-

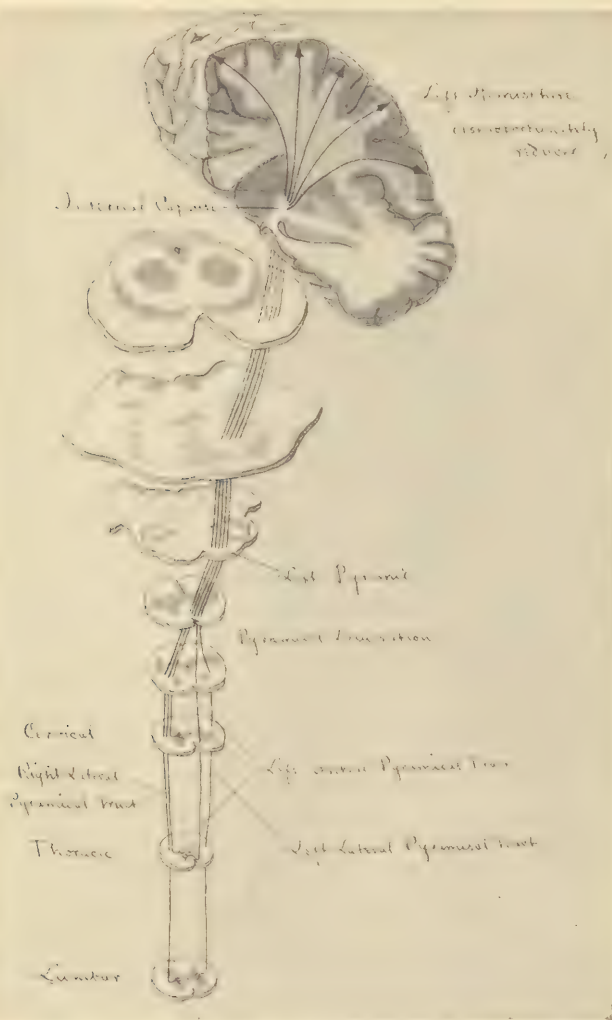


Fig. 18.—Origin and course of the ventral and lateral pyramidal tracts.

ing descend the lateral pyramidal tract end in the gray matter on the same side of the cord. By far the majority of the pyramidal fibers, then, cross in the medulla; of the remainder, the majority cross before they end; only a few end without crossing the median line. *Each half of the brain controls muscles on the opposite side of the body.* As the pyramidal tracts descend the cord they gradually diminish in bulk, for fibers leave them at each succeeding level to end in the gray matter. The ventral pyramidal tract disappears before reaching the lumbar region.

It is important to note that movement is not the only result of stimulating a given cortical area. If carefully localized stimulation be applied to the motor area for one set of muscles, the antagonists of this set relax; for example, stimulation of an area of flexion causes contraction of the flexor muscles concerned and simultaneous relaxation of the extensors which are antagonistic to them. The cortex can, therefore, both provoke and inhibit muscular contraction. Evidence of the removal of this **cortical inhibition** is seen on division of the pyramids: the spinal centers, released from control, respond more readily than usual to the afferent impulses which reach them from the periphery, and reflex muscular tone is exaggerated, the muscles are spastic.

Some of the motor fibers of the internal capsule which, on reaching the cerebral peduncle, lie medial to the fibers of the pyramidal tract, end in the motor nuclei of the cranial nerves, as is shown in Figs. 19 and 20. In addition, it appears that fibers descend through the median fillet, to end in the nuclei of the seventh and twelfth nerves.

EFFERENT FIBERS OF CRANIAL NERVES

The **third cranial nerve**, oculomotor, arises from a nucleus which consists of several cell-groups situated in the floor of the Sylvian aqueduct, at the level of the superior corpora quadrigemina. The most anteriorly situated cells of this nucleus appear to be concerned in **accommodation**; the next,

in **constriction of the pupil**; those innervating the **muscles of the eyeball**—namely, the inferior, superior and internal recti, and the inferior oblique muscles—and the **levator palpebræ** being situated more posteriorly. Some axons of the third nerve decussate before their exit, but the majority do not (Fig. 19).

The **fourth cranial nerve**, or trochlear nerve, arises from a group of nerve-cells which occupy much the same position as the nucleus of the third nerve, but are situated rather more posteriorly. The axons of these cells descend for a short distance before entering the velum, in which they cross to the opposite side, and emerge as the fourth nerve. This nerve innervates the **superior oblique muscle** of the eyeball (Fig. 19).

The smaller root of the **fifth cranial nerve** arises from two nuclei, the chief of which is situated in the dorsal portion of the pons; the other nucleus, that of the descending root, consists of a group of cells which are scattered over a narrow area, from the chief nucleus, forward, to the level of the corpora quadrigemina. The axons of these cells join the lower branch of the trigeminus and innervate the **muscles of mastication**. Cortical fibers, chiefly from the opposite hemisphere probably, reach the motor nucleus of the fifth nerve (Fig. 19).

The fibers of the **sixth cranial nerve**, or abducens, arise from a nucleus which is situated in the dorsomedial portion of the pons in the floor of the fourth ventricle. This nerve innervates the **external rectus** muscle of the eyeball. Cortical fibers reach this nucleus, chiefly from the opposite hemisphere (Fig. 19). This nucleus is brought under the influence of the superior corpus quadrigeminum through the posterior longitudinal bundle (Fig. 14). The same is true of the nucleus of the third nerve.

The **seventh cranial**, or facial nerve, arises from a nucleus situated ventrolaterally from that of the sixth nerve, and extending further posteriorly. The axons pass dorsomedially, and run for a short distance anteriorly beneath the floor of the fourth ventricle; they arch over the nucleus of the sixth nerve,

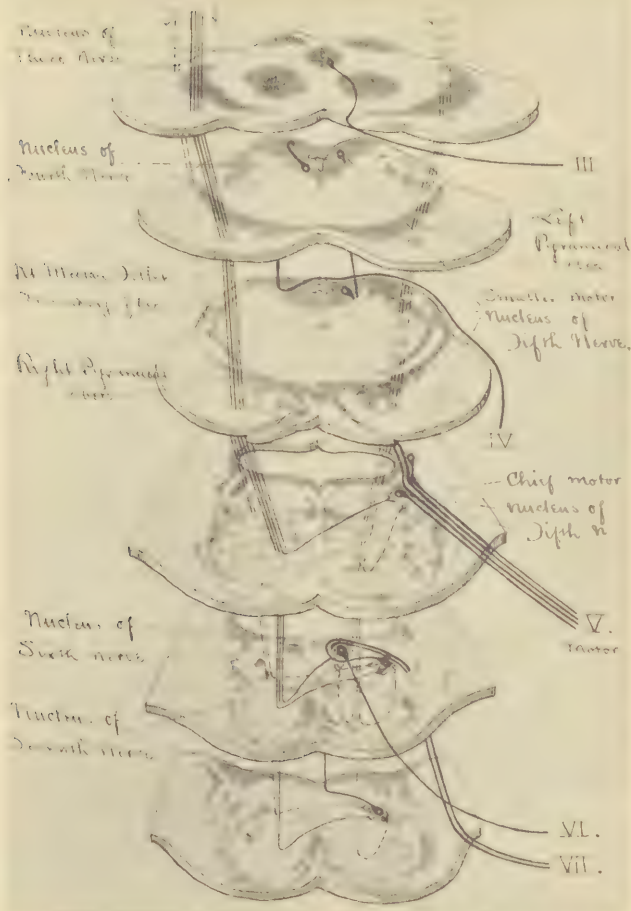


Fig. 19.—The efferent fibers of the third, fourth, fifth, sixth, and seventh cranial nerves.

and emerge ventrally from the lower border of the pons. This nerve is distributed to the **muscles of the face**. Corti-

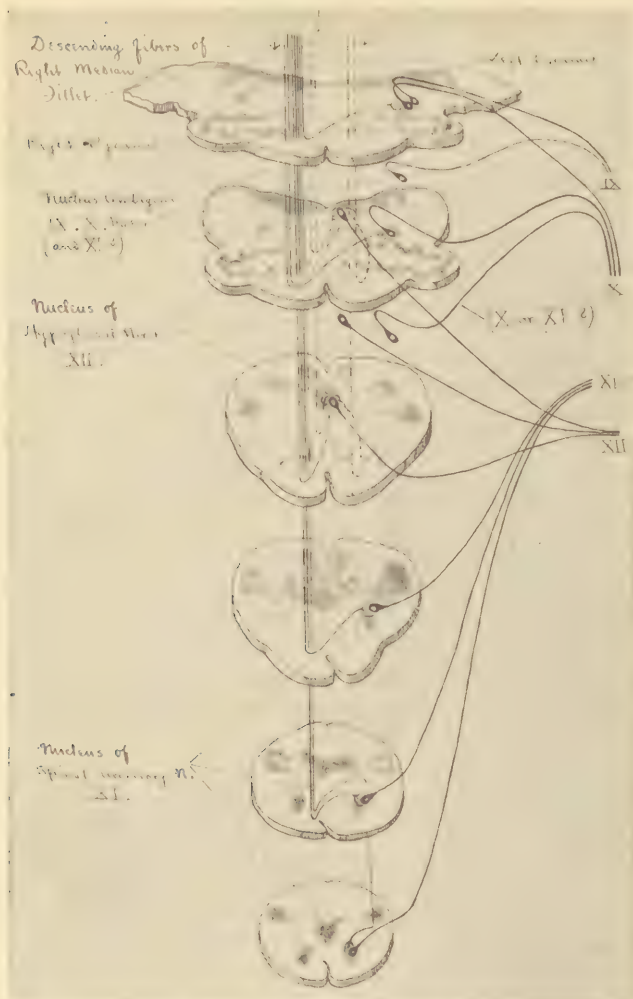


Fig. 20.—The efferent fibers of the ninth, tenth, eleventh, and twelfth cranial nerves.

cal fibers, chiefly from the opposite side, reach this nucleus; descending fibers of the median fillet also probably reach it (Fig. 19).

The motor fibers of the **ninth cranial**, or glossopharyngeal nerve, originate from the nucleus ambiguus, which lies in the reticular formation dorsal to the inferior olive. Its axons proceed dorsomedially, turn, and emerge in company with the afferent fibers of the nerve. The motor fibers of this nerve are distributed to the middle constrictor muscle of the pharynx and to the stylopharyngeus. This nucleus probably receives cortical fibers, mainly from the opposite side (Fig. 20).

The motor fibers of the **tenth cranial nerve**, vagus, or pneumogastric, also arise from the nucleus ambiguus, and its central connections are the same (Fig. 20). Its motor fibers are distributed to the pharynx and esophagus, larynx, bronchial muscles, stomach, and intestines. It also contains cardio-inhibitory fibers, and secretory fibers for the gastric glands and pancreas.

It is doubtful whether the cranial portion of the **eleventh nerve**, which also originates from the nucleus ambiguus, belongs in reality to this nerve or to the vagus, which it joins. The spinal portion originates from cells situated in the lateral horn of the cervical region, from the level of the first to the fifth or sixth cervical nerve. The spinal portion innervates the sternocleidomastoid and trapezius muscles. The nuclei of this nerve receive fibers from the opposite half of the brain, and possibly a few from the same side (Fig. 20).

The **twelfth cranial**, or hypoglossal nerve, is the motor nerve for the tongue, and arises from a nucleus which lies close to the median line in the dorsal part of the medulla; the upper end of this group of nerve-cells is just beneath the floor of the fourth ventricle; lower down it is ventral to the central canal. It receives fibers from the cortex cerebri, chiefly from the opposite side, and some descending fibers from the median fillet (Fig. 20).

THE CEREBRUM

The cerebral hemispheres are concerned in sensation, consciousness, memory, intelligence, and volition. The destruction of a **sensory area** (see Fig. 16) leads to loss of the sensation with which the area had to do; for instance, removal of the two occipital lobes results in complete blindness though the eyes are intact. Reflexes may still be carried on by paths which do not involve the cortex, as shown by the fact that the pupil will still contract when light is thrown into the eye. Destruction of a **motor area** (see Fig. 17) results in paralysis of the muscles which are innervated by this portion of the cortex. The paralyzed muscles may still be caused to contract in response to afferent stimuli, as this path does not pass through the cortex, but through the spinal cord. A unilateral cortical lesion affects but little the groups of muscles which act bilaterally, *e. g.*, muscles of inspiration. Such muscles seem to have a bilateral control.

The result of a complete **removal of the cerebral hemispheres**, which in some of the lower animals is possible, varies. The *frog*, deprived of its hemispheres, can, by its appearance, hardly be distinguished from a normal frog. It is capable of maintaining its equilibrium, of leaping and swimming, but shows not the slightest sign of memory or volition, and, save in response to some stimulus, never moves.

Pigeons bear the operation well, and their subsequent condition is similar to that of the frog. Undisturbed, they sleep most of the time; but if wakened, may walk about, clean their feathers, and if thrown into the air, fly. They must, however, be fed, for, lacking volition, they would otherwise starve to death. In time both the frog and the pigeon may begin to exhibit complicated reflexes that give the impression of intelligence.

In *dogs* the cortex can be completely removed only by successive operations. If this be accomplished and the animal be kept alive, it shows entire loss of intelligence and of mem-

ory, but is able to walk, and exhibits signs of sensation and emotion; the latter phenomena do not prove that the dog is conscious; they may be the expression of complicated reflex response to stimuli which are unperceived by the animal.

In *man* the extensive destruction of the cerebral cortex by accident or disease is usually followed by death; but small areas are often rendered functionless in this way, with the production of characteristic symptoms. The destruction of the motor areas on one side, as has been stated, results in paralysis of the corresponding muscles on the opposite side of the body; this may be accompanied by no loss of sensation. Destruction of the internal capsule, on the other hand, if it be complete, causes both motor and sensory paralysis of the opposite half of the body.

The well-being of the motor neurons concerned in voluntary movements is not all that is necessary to the proper use of our muscles. Movements in which but one muscle is brought into play are exceptional; as a rule, we use a group or several groups of muscles at one time, and the successful accomplishment of the movement is only possible if the contraction of the different members of the group be co-ordinated by the nervous system. **Co-ordination** is largely dependent on the reception of afferent impulses from the muscles themselves, and is consequently rendered imperfect by a break in the afferent pathway. Such is the case in tabes, in which the dorsal columns of the spinal cord are affected, and, consequently, muscle-sense is defective. In the lower animals the division of all the dorsal nerve-roots which innervate a limb leads to complete disuse of this member (apesthesia), though the motor pathway is in no way injured by the operation, and the muscles can be caused to contract by artificial stimulation of the motor cortical area.

If Figs. 16 and 17 be examined together it will be seen that by no means the whole of the cortex has been mapped out into motor and sensory areas; large cortical fields intervene, the stimulation of which leads to no visible result. These have been called by Flechsig **association areas**, and

are perhaps concerned with the interpretation of sensations, in memory, and with intellectual processes in general. There are several areas in the cortex of the left hemisphere which are intimately connected with the understanding and use of language. A lesion strictly confined to the left auditory area, though it causes deafness on the right side, may not interfere with the understanding of spoken language or with speech; but if the lesion is more widespread and includes the neighboring cortical area, the patient no longer understands the words which he can hear perfectly well with the left ear. The result seems to be due to an injury to an association area, rather than to the auditory area itself. The condition is one of **aphasia**.

The term "aphasia" means literally loss of the power of speech. We have extended this meaning and distinguish two varieties: **motor aphasia**, which consists in inability to produce speech, though not implying inability to cause the larynx to function as in speech; **sensory aphasia**, which consists in inability to recognize the meaning of words, though they may be heard with perfect distinctness. The term has been further extended to include similar disturbances in regard to written speech: **agraphia**, the motor variety, inability to write, though the hand innervation is intact; and **alexia**, the sensory variety, inability to understand the words which are read. These are all due to loss of memory of the muscular co-ordinations, or of the sensory associations, as the case may be. The areas involved are shown in Fig. 16. W is the area involved in agraphia; S, in motor aphasia; B, in alexia or word-blindness, and D, the area in sensory aphasia or word deafness. These conditions may be partial or single in their occurrence, depending on the site of the destructive lesion, or may occur in very varied combinations. A patient with motor aphasia may still, under the influence of emotion, be able to speak perfectly, or the power of singing speech may be retained. Left-handed individuals have these areas on the right side.

Not only are neighboring convolutions connected with one another by means of **association fibers**, but the different

lobes of each hemisphere are connected in the same way; in addition, the two hemispheres are united by association fibers through, for example, the corpus callosum. Stimulation of the corpus callosum causes, through indirect excitation of the cortical motor areas, bilateral movements.

The time that elapses between the reception of a stimulus which is responded to by a conscious volitional act is longer than the time of a reflex act. A *reflex* does not involve conscious cerebration, a *reaction* does. The **reaction time** occupied in any volitional response to an impression received is made up by the time occupied in the afferent and efferent paths, which are the same factors as enter into the time occupied in reflex acts plus the time needed to have the conscious perception recorded in the cerebrum, and to have the association of centers and co-ordination of efferent impulses take place, all of which processes take an appreciable time. In other words, it is possible to measure within certain limits the time taken in cerebration by subtracting the known time occupied in peripheral nerve processes from the entire time of a reaction.

THE CEREBELLUM

The voluntary control of movements, and more especially of those concerned in progression and in the maintenance of equilibrium, is very much interfered with by injury to the cerebellum. As we have seen, afferent impulses reach the cerebellum through the dorsal, direct cerebellar, and ascending anterolateral tracts of the spinal cord, and through the vestibular nerves from the semicircular canals; it also receives fibers from the inferior olives. It is, then, an important station for the reception of afferent impulses from a wide peripheral area. Nevertheless its destruction does not result in loss of sensation; the impulses which reach the cerebellum seem rather to be concerned in unconscious reflex co-ordination of muscular movement.

The patient who suffers from cerebellar disease, and, consequently, from inco-ordination of movement, is perfectly

aware, even when his eyes are closed, that his motions are ill directed, but lacks the power to order them rightly. With continued practice the defect may, to a certain extent, be overcome; but it would be quite impossible for such an individual to run downstairs; careful attention must be directed to each movement if it is to be carried out correctly.

Although the cerebellum is connected with the motor cells of the spinal cord by descending fibers, its influence on co-ordination seems rather to be exerted through fibers which ascend toward the cerebrum, and end either in the thalamus or in the cortex. The **vermis** is the portion of the cerebellum which is concerned in maintaining equilibrium. The function of the large lateral lobes is unknown, though it is possible that the lateral lobes are concerned in the memory of the muscular co-ordinations necessary for equilibrium.

The fibers which pass from the cerebellum to the cerebrum cross the median line in the superior peduncles, and end on the opposite side in the red nucleus or optic thalamus; from these bodies impulses are carried to the cortex by another set of neurons. Impulses pass in the opposite direction, from the cerebrum to the cerebellum, over fibers which connect the frontal and temporal cortex with the gray matter of the pons, and the gray matter of the pons with the opposite half of the cerebellum. The lateral vestibular nucleus, or Deiter's nucleus, probably acts as a relay station for the forwarding of impulses from the cerebellum to the gray matter of the spinal cord on the same side of the median line.

The motor symptoms which follow injury to one-half of the cerebellum appear on the side of the lesion; this is to be expected, since the fibers which leave the cerebellum transmit impulses, on the one hand, to the same side of the cord; on the other, to the opposite cerebral hemisphere; and, as we know, the cerebral control of a muscle is exercised by the opposite half of the brain.

THE SYMPATHETIC OR AUTONOMIC SYSTEM

This is a complicated system of nerves and ganglia quite outside of the central nervous system, though connected with it by afferent and efferent fibers. This autonomic system controls the function of the organs of the body over which we have no voluntary control, *e. g.*, heart, glands, plain muscle tissues. Though it is true that these organs may at times be influenced by voluntarily produced psychic states, this does not constitute an exception to the above statement, for the influence is not direct, but only a part of a reflex.

The sympathetic system comprises the two chains of **lateral or vertebral ganglia** extending from the superior cervical to the coccygeal ganglia on each side, and also the **collateral or pre-vertebral ganglia**, which include the celiac, superior mesenteric and inferior mesenteric ganglia in the abdomen, and the ciliary, otic, sphenopalatine, submaxillary, and sublingual ganglia in the head. Still other ganglia lie in and around various organs. Such are the cardiac and renal ganglia and the plexuses of Meissner and Auerbach.

As has been said this system is connected with the central nervous system by afferent and efferent fibers. The **efferent fibers** (Figs. 21, 22) are medullated and pass out with the cranial or spinal nerves, which they promptly leave to enter the ganglia. These are called **preganglionic fibers**. They end about the ganglion-cells, and the axons of these cells, for the most part non-medullated, pass on to the viscera. These are the **postganglionic fibers**.

Preganglionic fibers emerge in the *third* cranial nerve and pass to the ciliary ganglion, from whence the sphincter of the iris and the ciliary muscle are innervated. Fibers emerge in the *seventh* and *ninth* cranial nerves, and pass to the otic, sphenopalatine, submaxillary, and sublingual ganglia, supplying the glands and blood-vessels of the nasal and buccal mucosa and the salivary glands. With the *tenth* nerve, fibers pass to the smaller unnamed ganglia in the neighborhood of the organs. Their functions are motor to the musculature of

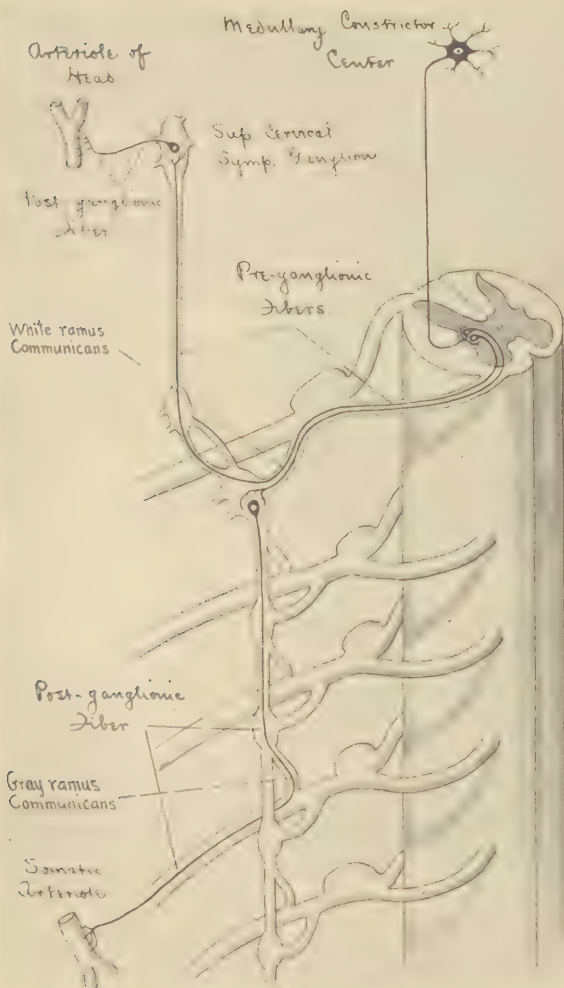


Fig. 21.—Course of efferent sympathetic fibers.

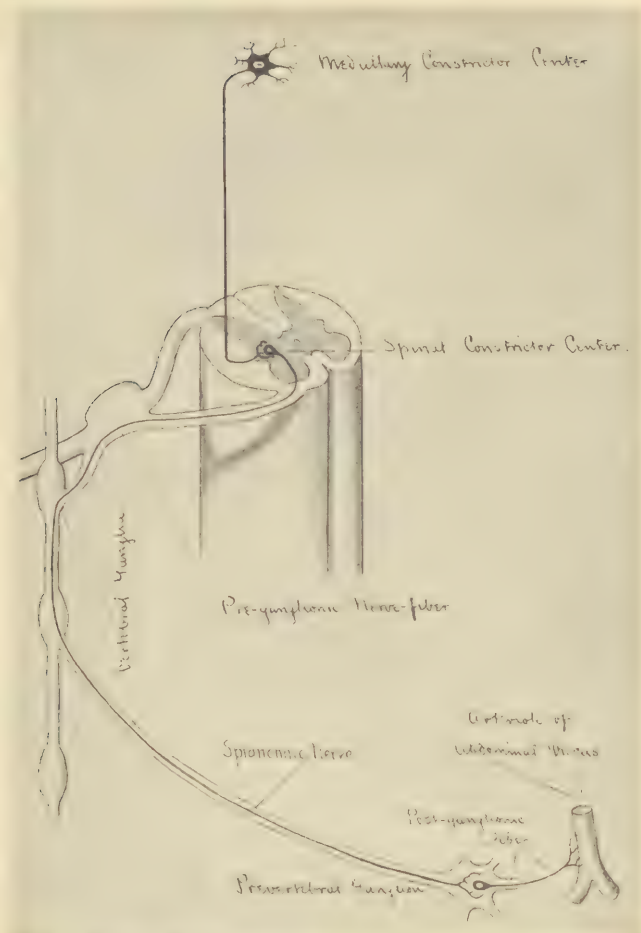


Fig. 22.—Course of efferent sympathetic fibers.

the esophagus, stomach, small intestine, large intestine as far as the ascending colon, and to the bronchi, inhibitory to the heart, and secretory to the gastric and pancreatic glands.

With the anterior roots of the *spinal nerves*, from the *first thoracic to the fourth lumbar*, preganglionic fibers emerge whose cells are situated in the gray matter of the cord, forming the intermediolateral group of cells. As these fibers leave the anterior roots to enter the gangliated cord they form the *white rami communicantes* (Fig. 21). These fibers do not always end in the first ganglion they enter, but may pass through several before doing so. The *gray rami communicantes* (Fig. 21) are composed of the axons of the cells of these ganglia, which pass back to the spinal nerves to be distributed with them to the blood-vessels of the skeletal muscles and skin and to the plain muscle and glands of the skin. Gray rami are found in connection with *every* spinal nerve. The preganglionic fibers for the head region all end in the superior cervical ganglion, while those for the abdominal and pelvic viscera form the splanchnic nerves which end in the celiac and superior mesenteric ganglia (Fig. 22).

Efferent fibers emerge in the *second to fourth sacral nerves* and unite to form the *nervus erigens*. They end in small ganglia in the pelvic plexus or near the organs supplied. The postganglionic fibers pass to the pelvic viscera and genital organs, their action being to dilate the blood-vessels of the genitals, rectum, and anus, and to contract the plain muscle of the descending colon, rectum, and anus.

Afferent fibers also connect the sympathetic with the central nervous system (Fig. 23). These pass by way of the posterior roots of the spinal nerves, and form a considerable part of the *vagus nerve*. The sensations which they mediate arise in the visceral organs, and just as the motor impulses to the viscera are not in consciousness so the normal sensations from the viscera are not referred in consciousness directly to the site of their origin. The pain resulting from visceral disease is due to overstimulation of these nerves, and is referred to the viscus, or to a definite area of the skin, this area being that which is supplied by the fibers of the same dorsal nerve-root which transmits the afferent fibers from the viscus. It seems that the afferent fibers entering the cord through a

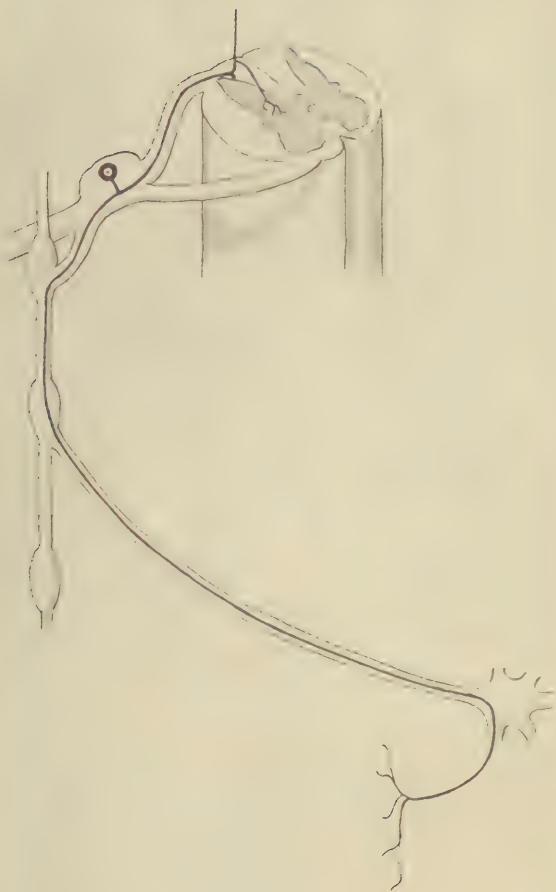


Fig. 23.—The course of an afferent sympathetic fiber.

given nerve-root make very similar connections with the brain, whether they are from the skin or the viscera. We are thus misled into confusing the sensations resulting from the unusual visceral irritation with those due to stimulation of a cutaneous area, whose afferent fibers discharge impulses at much the same point within the cord, and which do so more frequently.

The sympathetic system normally functions reflexly, and its processes do not enter into consciousness in any way. It is only when some abnormal condition arises that the afferent impulses from the viscera amount to sensations.

QUESTIONS FOR CHAPTER III

Compare the path followed by a motor-nerve impulse passing to a skeletal muscle with that of an impulse which reaches involuntary muscle.

How may we determine whether the ventral nerve-roots contain nerve-fibers which have descended the cord from a higher level?

How may we ascertain whether paralysis of a muscle depends upon injury to pyramidal fibers or to ventral root-fibers?

In what different ways may a nerve-center be directly influenced?

Injury to what different structures causes a loss of reflex contraction of muscle?

On stimulation of a motor cortical area, how many neurons are concerned in the transmission of the motor impulse to a muscle-fiber?

Having divided a nerve-trunk, what must be done to prevent permanent paralysis of the muscles innervated by this nerve?

How can you tell when a divided nerve has renewed its connection with a muscle?

Would you expect the paralysis which results from destruction of the gray matter of the cord to be permanent or otherwise?

To what extent is the voluntary use of muscles affected by division of the posterior nerve-roots?

How can we decide, by the examination of a section of the upper cervical cord, whether degeneration found in the dorsal column was the result of a lesion situated in the lower cervical or lower thoracic region?

Given three animals, A, B, and C, the left internal capsule of A having been destroyed, the left half of the spinal cord of B having been transversely divided in the thoracic region, and in C all the lumbar and sacral posterior nerve-roots having been divided, explain the effect in each case, if any exist, on the voluntary movements of the left leg and on the left knee-jerk.

How can we ascertain, from the nature and distribution of sensory paralysis, whether the causative lesion is situated in the internal capsule or consists in hemisection of the cord?

What lesion will bring about loss of voluntary movement of the leg and exaggeration of the knee-jerk?

Explain the difference between white and gray rami communicantes.

What is the numerical difference in the neurons concerned in an efferent and an afferent nerve impulse through the sympathetic system?

What lesion will cause inco-ordination of voluntary movement and loss of the knee-jerk?

How can we determine the level of a lesion of the cord which has brought about paralysis of the leg?

Will a lesion of the cord which causes paralysis of the legs necessarily result in paralysis of their arterioles?

How do the results of injury to the ventral nerve-roots differ, with regard to muscular contraction, from those arising from injury to the dorsal nerve-roots?

Where do peripheral sensory nerve-fibers originate?

In respect to voluntary contraction, reflex contraction, and sensation, how do the effects of the following lesions differ: Destruction of the motor cortical area on one side; destruction of the internal capsule on one side; division of the pyramid of the medulla; and hemisection of the cord in the lower cervical region?

What comment have you to make on a case in which loss of speech accompanied paralysis on the left side of the body?

How may an animal be blinded without destroying visual reflexes?

What lesions will lead to a loss of the pupil light-reflex without causing blindness?

What is the result of injury to or removal of the semicircular canals?

What are the distinguishing points as to time and nerve path between a reflex act and a reaction?

CHAPTER IV

THE SPECIAL SENSES

WE distinguish plainly in consciousness certain sorts of sensations—touch, pain, temperature, sight, hearing, smell, and taste. Certain other sensations we are less plainly conscious of under normal conditions, unless we direct attention carefully toward them—motion, position in space, tension of the muscles, visceral sensations, hunger, thirst, sexual sense, and fatigue. It will be noted that in general these groups are due to stimuli extraneous to the body in the first case—the **external sensations**—and inherent in the body in the second—the **internal sensations**.

We have seen that the nerve impulse is the same in all nerve-fibers, no matter what their function. The facts which determine what sensation shall result when an afferent nerve is stimulated artificially are the central connections of the fibers, or the portion of the cerebral cortex which the impulse ultimately reaches. Whether that nerve can be stimulated physiologically depends upon the quality of its end-organs, *i. e.*, whether or not they react to the type of stimulus used. The skin cannot mediate light sensations nor the retina sound. These facts have given rise to the **Doctrine of specific nerve energies**, which holds that each sensory unit mediates only its own peculiar type of sensation. An important fact in regard to the external sensations is expressed by **Weber's law**: that the amount of stimulus necessary to be appreciated as an increase in the sensation is always a constant fraction of the amount of stimulus already applied. Small increments are appreciated with a small initial stimulus, but as the stimulus is increased, the increments must be increased proportionately.

CUTANEOUS SENSATIONS

These include the sensations of touch, heat, cold, and pain. Each sensation arises by stimulation of definite end-organs in the skin, which are sensitive to only one form of stimulus. If care is used to test with a pointed instrument, these sensations can be shown to have a *punctiform distribution*.

The nerve-endings for pain are most numerous, touch being next in order and heat least numerous.

The sense of *touch* varies greatly in different parts of the body as to its acuteness, *i. e.*, the minimal stimulus necessary to cause a sensation, and also as to the degree of separation necessary that two points may be appreciated as such. *Heat* and *cold* are appreciated as variations from the existing skin temperature, whatever that may be, the intensity of the stimulus varying according to Weber's law. The *pain* endings react only to stimuli of greater intensity than those causing the other sensations in the region in question. All of the sensations are referred quite accurately to the portion of the body's cutaneous surface affected, but for each sensation, and for each cutaneous surface, there is a limit of nearness beyond which two stimuli side by side cease to be perceived as two; this may be said to form an area within which we cannot localize sensation.

The *mucous membranes* of the nose, mouth, pharynx, anus, and rectum also have nerves of touch and temperature, but the *viscera* are supplied only with nerves of pain, and that very sparingly. Under afferent fibers of the sympathetic the inexact localization of visceral pain has been mentioned.

SIGHT

When light passes from one medium into another the density of which differs from that of the first, the course of those rays which do not fall perpendicularly upon the surface of the second medium is changed—the rays are refracted. As light enters the eye, it passes from the air into the cornea, then

into the aqueous humor, then into the lens, and, traversing the vitreous humor, reaches the retina. It thus passes through four curved refracting surfaces on its way to the retina—namely, the anterior and posterior surfaces of the cornea, which are parallel to one another; and the anterior and posterior surfaces of the lens, which are parallel neither to the corneal surfaces nor to each other. The centers of curvature of all these surfaces are, however, situated approximately upon one axis, so that a ray of light traveling along this axis will suffer no refraction on its way to the retina; this is called the *principal axis*. Other rays which enter the eye will be refracted at each of the four surfaces which they traverse.

The extent of refraction depends upon the course of the ray, the curvature of the surface, and the difference in the density of the two media separated by the surface. The more obliquely a ray of light cuts the refracting surface, the greater the curvature of the surface, and the wider the difference between the density of the media, the greater will be the degree of refraction. Considerable refraction occurs at the anterior surface of the cornea, where the light passes from the air, the refractive index of which is 1.0, into the cornea, the refractive index of which is 1.37, its radius of curvature being 7.8 mm. Very little refraction occurs at the posterior surface of the cornea, since the refractive index of the aqueous humor (1.33) differs but little from that of the cornea. The refractive index of the lens is 1.43, the radius of curvature of its anterior surface being, when the ciliary muscle is at rest, 10 mm.; here, again, the refraction is considerable. The rays are again refracted at the posterior surface of the lens, the radius of curvature of this surface being 6 mm.; here the rays pass into the vitreous humor, the refractive index of which is the same as that of the aqueous humor (1.33).

This complex system of media and refracting surfaces may, however, be represented by what is known as the **reduced eye**, which consists of one medium with an index of refraction the same as that of the aqueous and vitreous humors, bounded by

one surface with a radius of curvature of 5.1 mm, and lying 2 mm. behind the anterior surface of the cornea. The nodal point or optical center of this eye lies 15.5 mm. anterior to the retina. The refraction suffered by a ray of light on entering such an eye would be equal to the total refraction suffered, on its way to the retina, by a ray forming the same angle with the principal axis of the normal eye. Such a reduced eye represents the physical facts of the normal eye only when the ciliary muscle is at rest. The refracting surface of a reduced eye that shall accurately represent the refraction that occurs in the normal eye when the ciliary muscle is contracted must have a greater curvature.

Rays of light the course of which is parallel to the principal axis are refracted to meet, at the *posterior principal focus*, on the principal axis; when the ciliary muscle is at rest, the posterior principal focus falls upon the retina. The anterior principal focus lies 12.9 mm. in front of the cornea, on the principal axis; rays which emanate from this point are, within the eye, rendered parallel to the principal axis. The cardinal points of the system are the anterior and posterior principal foci and the nodal point.

Rays of light which fall perpendicularly upon the refracting surface of the reduced eye suffer no refraction, but pass on through the nodal point to the retina. Consequently, a ray of light emanating from a point above the principal axis and falling perpendicular to the refracting surface will reach the retina at a point below the principal axis; a ray coming from a point situated below the principal axis will strike the retina above it, and similar relations are true for rays coming from either side.

The formation of an image on the retina is shown in Fig. 24. With the exception of the principal ray (*P. R.*), which falls perpendicularly upon the refracting surface of the reduced eye (this surface is represented in the figure by a broken line), the diverging rays which are reflected from a given point of the surface of an opaque object, and which enter the eye, are refracted to meet the principal ray upon the retina, and form

here an image of the point from which they were reflected. In like manner, there are formed images of other *equidistant* points of the object at the points where their principal rays strike the retina. In this way an image of the whole object may be formed; it is, of course, inverted. Although the retinal images are inverted and reversed as to their lateral relations, yet we do not see the object reversed because the retinal image never enters consciousness as such. Our brain projects sensations from the upper part of the retina to a level below the plane of our visual direction, proportionally as the stimulus lies above the center of the retina, and this is true in a similar

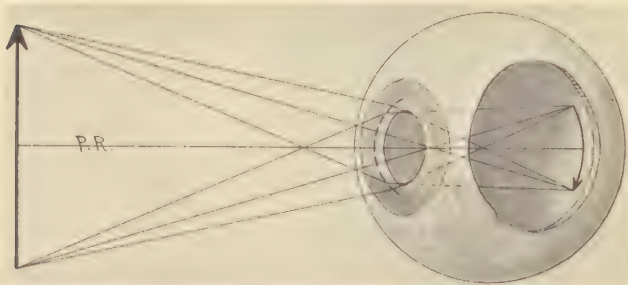


Fig. 24.—Formation of an image on the retina.

way for all other points of the retina. If the inner and lower portion of the eyeball be stimulated mechanically, the resulting sensation—a series of blue and yellow rings—will be perceived as occurring in the upper and outer part of the field of vision.

When the ciliary muscle of the eye is at rest, rays of light which diverge from a point near the eye are not, by the time they reach the retina, brought to a focus; consequently, they form, instead of a sharp image, a diffusion circle. In order that a sharp image of a near object may be formed on the retina, the focal distance of the eye must be shortened. This is known as **accommodation**, and is accomplished by the con-

traction of the **ciliary muscle**. When this muscle is at rest, the lens is flattened by the tension to which the suspensory ligament and capsule are subjected owing to intraocular pressure. When the ciliary muscle contracts, it stretches the elastic choroid coat, and pulls forward its anterior margin, to which is attached the suspensory ligament. The suspensory ligament and capsule being thus slackened, and the pressure on the enclosed lens being reduced, the anterior surface of the elastic lens bulges forward, its curvature is increased, and, with the curvature, the power of refraction. The image of an object which is near the eye may thus be formed upon the retina. The normal eye cannot, however, be accommodated for objects which lie within 10 or 12 centimeters of the cornea. This is known as the near-point of distinct vision. Since parallel rays are brought to a focus upon the retina of the resting eye, the far-point of vision is at an infinite distance, though practically all objects at a distance of 20 or 30 feet are in focus without accommodation, for the rays from such a distance are all so nearly parallel that the difference in focus is not appreciable.

The **nervous mechanism** of the eyeball is quite complicated. Efferent sympathetic fibers to the eye pass from the *third nerve* to the ciliary ganglion, and thence as postganglionic fibers, through the short ciliary nerves, to the ciliary muscle and the sphincter pupillæ. Other fibers emerge in the eighth *cervical* and *first and second thoracic* spinal nerves and pass through the first thoracic ganglion to the superior cervical ganglion, where they end. Postganglionic fibers pass from here to the Gasserian ganglion, and, traversing its ophthalmic branch and the long ciliary nerves, innervate the dilator pupillæ. These three muscles are maintained in a condition of tone by constant nerve impulses along the paths mentioned, so that interruption of the impulses at any point will be shown by relaxation of the corresponding muscle. The ciliary muscle can to some extent be voluntarily contracted, so that we can focus for near objects without fixing the vision upon an object. Whether this is true voluntary control, or is a reflex induced

by the psychic state of "viewing a near object" which is present in consciousness, is possibly an open question.

Accommodation is always accompanied by contraction of the pupil, thus diaphragming the lens, and by cutting out the peripheral rays, improving the focus. This is called the **accommodation reflex**, but is, in reality, an associated movement. The voluntary act of accommodation affects the medullary centers, for both of these act simultaneously. The **light reflex** is, however, a true reflex, the afferent path being from the retina through the optic nerves and tracts to the anterior corpora quadrigemina, and thence to the nucleus of the third nerve where the efferent impulse originates. The paths involving the dilator pupillæ in this reflex are not known. By the light reflex the pupil is constricted when the retina is too strongly illuminated, thus decreasing the amount of light entering the eye and improving the retinal image by reducing spheric aberration. In dim light the pupil is widely dilated, thus allowing the maximum illumination of the retina. Constriction of the pupil is called *miosis*, and dilatation is called *mydriasis*.

Both accommodation and the size of the pupil are affected by certain drugs; atropin, for example, paralyzes the terminations of the motor nerve-fibers of the ciliary and constrictor muscles, and probably stimulates the fibers which cause dilatation; physostigmin, on the other hand, stimulates the terminations of these nerves and paralyzes the dilators. Emotional states may also cause mydriasis.

The eye being an optical system may have certain inherent optical defects. A normal eye, which has none, is spoken of as **emmetropic**. In the **myopic**, or short-sighted eye, the posterior principal focus falls in front of instead of upon the retina. In the **hypermetropic**, or far-sighted eye, the posterior principal focus lies behind the retina. The former condition usually results from an abnormally great anteroposterior diameter of the eyeball, the latter condition from this diameter being too small. With accommodation relaxed the *myopic* eye focuses distant objects in front of the retina, *i. e.*, too soon,

so that the far-point for distinct vision is nearer than in a normal eye; distant objects *cannot* be seen clearly. Its maximum accommodation though will allow it to bring to a focus on the retina objects which are nearer to it than a normal eye can. Larger images of nearby objects can thus be formed on the retina; near vision is more acute than normal. Without accommodation the *hypermetropic* eye has no far-point of distinct vision, for parallel rays from distant objects are not yet focused when they reach the retina and the diverging rays from nearer objects are focused still further back of the retina. This condition though may be compensated for to a certain extent by accommodation, so as to bring far objects (parallel rays) in focus on the retina. The maximum accommodation cannot, however, focus objects as near by as can the emmetropic eye; the near-point is accordingly further away than normal.

As age advances, the power of accommodation is impaired, through weakness of the ciliary muscle and lessening of the elasticity of the lens, the condition being known as **presbyopia**; the *near-point* of distinct vision thus gradually recedes from the eye, but there is no interference with the vision of distant objects.

Astigmatism is an imperfection of vision which is usually dependent on differences in the curvature of the cornea. In the commonest form the curvature of the cornea is greater in the vertical than in the horizontal meridian, and, as a result of this, the rays which, diverging from a given point, fall upon the vertical meridian of the cornea, are brought to a focus earlier than those which fall upon the horizontal meridian. Consequently, when the eye is so accommodated that the anterior of these two foci falls upon the retina, the image formed will be, instead of a point, a horizontal line, for the rays in the vertical plane are focused, but in the horizontal plane they are not yet focused. If the posterior focus falls upon the retina, the image will be a vertical line for a similar reason (Fig. 25). Almost every eye is more or less astigmatic, and none are free from defects.

One constant defect consists in **spheric aberration**, which depends upon the fact that rays falling upon the periphery of the lens are more refracted, and brought to a focus earlier, than those which fall nearer to the principal point. This effect is, however, to a certain extent, neutralized by the curvature and index of refraction of the peripheral portion being less than is the case with the more central portion of the lens. The iris, too, forms a diaphragm which prevents light from falling on the periphery of the lens, and this is of special importance in the case of the more divergent rays which reach the eye from near objects; as we have seen, the iris contracts when near objects are viewed. **Chromatic aberration** is caused by dispersion due to the unequal refrangibility of rays

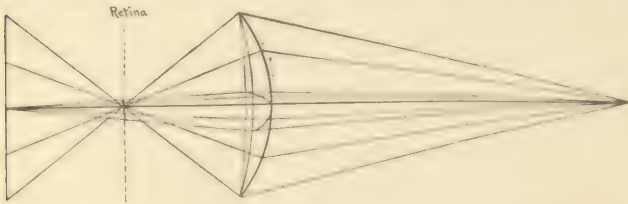


Fig. 25.—Illustrating astigmatism.

of different wave-length; those of shorter wave-length, *e. g.*, violet rays, are more refracted than those of greater wave-length, the red rays. Under ordinary circumstances neither spheric nor chromatic aberration interferes with distinct vision.

The eye maintains its spheric shape, owing to the fact that the fluid within the sclerocorneal sac is under a certain tension. This tension is maintained in part, at least, by filtration from the capillaries in the ciliary processes. If the tension is too great, the fluid drains off through the canal of Schlemm. Thus the tension may be increased by a rise in blood-pressure or by a blocking of the canal of Schlemm, either of which may occur in pathologic states. Increased intra-ocular tension is called **glaucoma**.

Color Vision.—White light on analysis is found to consist of a mixture of rays of varying wave-length. When light falls upon the retina, the resulting sensation varies with the wave-length of its component rays. According to the **Young-Helmholtz theory**, there are in the retina three photochemical substances, all of which are to a certain extent acted upon by any ray of light, whatever its wave-length; but the readiness with which each substance reacts to different rays varies. For instance, rays the wave-length of which is in the neighborhood of 0.000675 mm. affect one substance more than the other two, and give rise to a sensation of red; rays of about 0.000525 mm. wave-length produce the greatest effect on the second substance, and give rise to a sensation of green; rays of 0.000430 mm. wave-length cause the greatest change in the third substance and result in a sensation of violet. A sensation of yellow results from the simultaneous production of red and green sensations in certain proportion; a sensation of orange is produced by slightly increasing the red sensation and lessening the green. Thus a host of different color sensations may be produced by the fusion of the primary sensations in varying proportions. The sensation of white results from the fusion of all three primary sensations in definite proportions; this is what occurs when ordinary daylight falls upon the retina, but to produce this result it is not necessary that all the rays of the visible spectrum should enter the eye. Any two rays which between them excite all three color sensations in the right proportion will give rise to a sensation of white; for instance, a ray of the wave-length 0.000564 mm., when it alone reaches the retina, causes a sensation of greenish yellow by acting about equally on the visual substances concerned in red and green sensations; if to this ray be added one of the wave-length 0.000433 mm. which by itself causes a sensation of violet by acting to about the same extent on the third substance, a sensation of white will result. Every ray situated toward one end of the spectrum has its complementary ray, found toward the opposite end, combination with which gives rise to a sensation of white. Rays near the middle of the

spectrum which give rise to a sensation of green require to be combined with rays from both ends of the spectrum in order to cause a sensation of white. A sensation of black is caused by the absence of any stimulus.

There are certain facts in color vision which cannot be satisfactorily explained on this theory, and in consequence several others have been advanced; to all these there are, however, objections. According to the **theory of Hering**, there are six primary color sensations, depending on anabolic or katabolic changes in three visual substances. In one of these substances katabolic changes may be excited by the rays of any part of the visible spectrum, and a sensation of white results; in the absence of light, anabolic changes predominate and give rise to a sensation of blackness. Another substance is caused to break down by the rays of greater wave-length, giving rise to a sensation of red, while it is rapidly built up under the influence of the rays of medium length, with a resulting sensation of green. The third substance suffers katabolic changes under the influence of rays which produce sensations of yellow, and undergoes constructive changes when exposed to the rays of shorter wave-length which produce a sensation of blue. When rays of all wave-lengths fall upon the retina, the metabolism of only the "white-black" substance is affected; the other two substances remain in equilibrium. Orange sensations result from the simultaneous break-down of the red-green and yellow-blue substances, violet sensations from the simultaneous building up of yellow-blue and break-down of red-green substance.

The **Franklin theory**, probably the most satisfactory, supposes but one photochemical material, which when broken down by the ether vibrations gives rise to sensations of gray of varying intensity. In the region of the retina capable of perceiving color this substance is supposed to be arranged in certain specific molecular groupings, so that it may be dissociated only in part. The more rapid waves break down one group and cause a blue sensation; the slower waves break down the other and cause a sensation of yellow. In certain

regions this yellow-perceiving substance is also arranged in a double grouping; the one part which is affected by the longest visible waves gives rise to a red sensation, while the other is dissociated by the waves which cause a sensation of green. It is to be noted that simultaneous destruction of red and green will produce yellow, and of yellow and blue or of red, green and blue will produce gray.

The objection to all these theories is that they necessitate the possibility of qualitative variations in the impulses along the optic nerve, a thing physiologists are very loath to admit.

Color-blindness appears to depend upon the existence in the retina of the individual of but two visual substances. As a rule, those who are color-blind fail to distinguish between red and green; this may be explained on the Young-Helmholtz theory, by supposing either the "red substance"; or the "green substance" to be absent from the retina; on Hering's theory by the absence of the "red-green substance;" and on Franklin's theory by supposing that the yellow substance is incapable of further molecular arrangement. The periphery of the retina is entirely color-blind, and just within this area is one where only blue and yellow can be perceived. Only the central part of the retina can perceive all colors.

Visual Sensations.—When light falls upon the retina, it affects both the pigment epithelial cells of the outer layer and the rods and cones; visual sensation depends upon stimulation of the latter elements, and it results whatever be the nature of the stimulus. Pressure when applied to the eyeball affords mechanical stimulation of the retina, and a visual sensation follows.

The retina may also be stimulated electrically, with the production of visual sensations.

Different parts of the retina are not equally sensitive to light, and a variation in the quality of light affects them differently. We can most accurately distinguish between closely adjacent points when their images fall upon the **macula lutea**, or fovea centralis; in this respect acuteness of vision gradually diminishes as the periphery of the retina is approached. The

same is true in respect to color vision; the extreme periphery of the retina is color-blind. On the other hand, the macula lutea is not the part of the retina that is most sensitive to dim illumination. Rods are absent from the macula lutea, cones only being present; as the periphery is approached, the number of rods increases, the number of cones diminishes, and before the border is reached the cones disappear. It seems probable that the cones are chiefly concerned in acute vision and in color vision, while the rods minister to the perception of luminosity without, perhaps, affording a means for the appreciation of color. The rods contain a substance, **visual purple**, which is absent from the cones, and it may be owing to the presence of this substance that the rods are most readily stimulated by rays of light of slight intensity. Visual purple is rendered colorless by exposure to light, but during the process an intermediate substance, a pigment called visual yellow, is formed. On exclusion of light, visual purple again slowly appears in the rods, but not in the absence of the layer of pigment epithelium, which evidently exerts an influence on its formation. This increase of visual purple in the absence of light seems to be the reason that the eye "becomes accustomed to the dark," after the light has been excluded or greatly diminished for a time.

The **optic disk**, that part of the retina where the fibers of the optic nerve leave the eye, is devoid of rods and cones and is blind. Of this defect we are unconscious, until it is pointed out to us that with but one eye open the image of an object which falls upon this area is unseen.

The blind spot does not appear as a dark area, but as an absent area, so that no gap appears in our consciousness of the visual field. It is projected outward at an angle of about 25 degrees lateral to the point of fixation of each eye, so that the image of an object can never fall simultaneously on the blind spots of both eyes.

When light falls upon the retina, the effect on consciousness varies with the intensity of the light, with the duration of the exposure, with the size of the retinal area illuminated,

and with the condition of the retina. The excitability of the retina is reduced by exposure to light; it becomes fatigued, and visual sensations are less intense; this probably also depends upon fatigue of the central visual mechanism. In order to excite visual sensation, light, must be of certain intensity, this intensity varying with the part of the retina upon which it falls, as has been already mentioned. Weber's law of the perception of proportional increments holds good here also, so the brighter the light, the more difficult it is to appreciate small variations in intensity (the minimal perceptible variation is 0.01 of the initial illumination).

A flash of light may appear less bright than a somewhat weaker light that lasts longer. A small light may appear less luminous than a larger one which is, in reality, of less intensity. Since the sensation outlasts the stimulus by a short period, a rapid succession of stimuli of very short duration gives rise to a continuous sensation. The survival of a visual sensation after the stimulus has ceased is known as a positive **after-image**. Negative after-images are fatigue phenomena; for instance, if after fixing the eye for a few moments upon a red object it is turned to a white surface, there appears a greenish image of this object; this is explained by assuming that in the area of the retina upon which the rays from the red object fell the visual substance upon which the red rays take most effect has been used up or rendered inexcitable to a greater extent than either the green or the violet-perceiving elements; consequently, when the whole retina is subsequently exposed to white light, which excites all three primary sensations, the two which have not been fatigued will predominate, and we experience a sensation of greenish-blue. The color of a negative after-image is always complementary to that of its original.

When two objects the colors of which are complementary to one another are placed in contact, the color of each, more particularly along the adjacent edges, appears to be intensified. This may be explained by assuming that stimulation of any retinal area causes simultaneous changes to occur in

neighboring areas; by some, these induced changes are supposed to be similar to those occurring in the stimulated area; by others, they are considered to be of an opposite nature.

A white object on a dark field looks larger than it does on a white field; this is called **irradiation**, and depends upon the failure of the eye to bring all the rays to a proper focus, the size of the retinal image being slightly increased through the formation of diffusion circles instead of points at the border of the white object.

Movements of the Eyeball.—To each eyeball are attached **three pairs of muscles**, the two members of each pair being antagonistic to each other. The movements of the two eyes are associated in such a way that their visual axes are kept parallel to each other when directed toward distant objects. During accommodation the visual axes converge. In what is known as the primary position of the eyes, the visual axes are parallel, and, the head being erect, are directed toward a distant point at their own level. The center of rotation of the eyeball lies 13.54 mm. behind the anterior surface of the cornea **on the optic axis**.

The optic axis does not exactly correspond to the visual axis, but cuts the retina on the inner side of, and slightly above, the macula lutea. Rotation of the eyes from the primary position to the right is caused by contraction of the right external rectus muscle and left internal rectus; horizontal convergence is caused by contraction of the two internal recti. Upward rotation is brought about by the simultaneous contraction of the superior recti and inferior oblique muscles; downward rotation, by the simultaneous contraction of the inferior recti and superior oblique muscles. More than two muscles must act upon each eye in order to bring about oblique upward or downward movement; this is accompanied by more or less wheel movement, or rotation on the optic axis. The voluntary contraction of one muscle is accompanied by **inhibition of its antagonist**.

As long as, through the associated movements of the two eyes, the visual axes are directed toward the same point, an

image of this point will fall upon the macula lutea of each eye and will give rise to a single sensation. The maculæ luteæ are not the only areas of the retina simultaneous stimulation of which gives rise to a single sensation; each retinal area, with the exception of those near the nasal edges of the retina, has a **corresponding area** in the opposite retina. When the two retinal images of an object fall upon corresponding areas the object appears single; when the images fall upon areas which do not correspond the object appears to be double. Slight asymmetry in the position of images falling upon *peripheral areas* of the retina does not so readily cause diplopia (double vision) as does the asymmetric arrangement of images on the maculæ luteæ. This is partly because in the periphery the vision is not so acute and small variations are not perceived, but chiefly because our consciousness is directed upon the object focused on the macula.

We first learn to interpret our visual sensations through comparison with sensations provoked through other channels. Our **visual judgment** of the size of an object is formed by comparing the sensation which it excites with those produced by other objects with which we are familiar, and if the object be large by the angle through which the eye must be moved in order to cover its surface. The movements of the eye are estimated partly through the intensity of the effort expended in causing the contraction of the ocular muscles, and partly through the muscular sensation resulting from their contraction. The distance of an object may be much more accurately determined by using both eyes than by using only one; in the case of a near object, the degrees of accommodation and of convergence are important aids to judgment of distance. It is difficult to form an idea of the shape of an unfamiliar solid object by means of one eye, but since, when both eyes are used, it is viewed from two points, the retinal images differ slightly and we are enabled to appreciate its depth.

HEARING

Sound-waves that enter the external auditory meatus cause vibration of the tympanic membrane, and are transmitted through the chain of ossicles, which vibrate as a whole to the perilymph of the internal ear. The vibration of the perilymph is transmitted to the endolymph of the membranous labyrinth, and in some way takes effect on the terminations of the nerve-fibers of the auditory branch of the eighth cranial nerve. Pressure on the two sides of the tympanic membrane is equalized by the communication which exists between the middle ear and the pharynx by means of the Eustachian tube; uneven pressure would interfere with the vibration of the membrane.

The vibrations which give rise to a musical sound are rhythmic; a noise results from arrhythmic vibrations. Sounds vary in **intensity**, or loudness, in **pitch**, and in **quality**. Intensity depends upon the amplitude of the vibration; pitch, upon the rate of vibration. A single sound emitted by a musical instrument is usually not simple, but compound, and this depends upon the admixture of overtones with the fundamental tone. The same note produced by different instruments differs in quality, owing to variation in the number and intensity of accompanying overtones. When two sounds occur simultaneously the vibrations upon which they depend do not reach the ear separately, but are fused and form a compound wave; nevertheless, we are capable of analyzing a complex sound. The ear probably contains a system of resonators, which, like the strings of a harp or other instrument, are caused to vibrate when subjected to the influence of sound-waves, each resonator responding to a tone of definite pitch. The basilar membrane of the cochlea, with its thousands of radial fibers of different lengths, perhaps serves as a system of resonators in the analysis of sounds, the vibration of each fiber being communicated, through the organ of Corti, to a particular nerve-fiber of the auditory nerve.

The ear shows a *specific selective action* for certain ranges of

pitch. It is much more sensitive to waves with a vibration frequency of between 4000 and 25,000 per second than above or below these pitches, so that lower or higher pitched sounds must have more intensity in order to be heard. Sounds of less than 400 vibrations per minute must be of considerable intensity to be heard, while at 25 vibrations is usually found the lower limit of hearing. Slower frequencies are felt as vibrations of the air, not heard as sound.

Our aural judgments are much less exact than our visual judgments, and even by the use of both ears it is difficult to determine whence a sound reaches us. This is especially true of sounds which emanate from a point in the median vertical plane. It is less difficult to locate sounds whose source of origin is lateral to the head, for, in this case, the intensity, and perhaps the quality of the sound, as it reaches the two ears varies. If sounds succeed each other with but a brief interval, the sensation may be continuous.

EQUILIBRIUM, MOTION, AND POSTURE

The Semicircular Canals.—The afferent impulses which pass from the semicircular canals to the central nervous system are of the utmost importance in the conscious appreciation of the movements of the body as a whole, and of its position, and in the reflex and voluntary maintenance of equilibrium. The nerve-fibers which enter the medulla through the vestibular nerve are the central axons of the bipolar vestibular ganglion-cells; the peripheral axons (or dendrites?) of these cells are distributed to the macula acustica of the utricle and to the cristæ ampullares of the semicircular canals. In these structures the fibers branch, their terminal fibrillæ surrounding the bodies of the hair-cells. The hair-cells are so called on account of the hair-like processes which project from their free surface into the endolymph which fills the membranous labyrinth.

The semicircular canals on each side are arranged in the three planes of space, at right angles with one another; conse-

quently, the head cannot be moved without causing, in one or other of the canals, a change in the pressure which is exerted by the endolymph on the hair processes of the epithelium. Further, the relations existing between the arrangement of the canals on the two sides of the head is such that each canal has a corresponding one on the opposite side which lies in a parallel plane. These parallel canals have their ampullæ at the opposite ends, so that a change of pressure on the hair processes in one ampulla is accompanied by a change of pressure in the opposite direction in the ampulla of the parallel canal on the opposite side. Changes of pressure on the hair-cells cause stimulation of the terminations of the vestibular nerve-fibers, and these transmit impulses to the medulla. The central connections of these fibers have been discussed. Disease of or injury to any of the semicircular canals may cause **vertigo**; but if all the canals on one side are removed there will be marked loss of equilibrium and muscular co-ordination, resulting in a falling to the affected side. The canals seem to function as a *dynamic* organ of equilibrium, giving us the sensations which guide our movements. In this connection their close anatomic connection with the cerebellum is of interest.

The **utricle** and **sacculæ** each have a small collection of hair cells, and lying in the interstices of the hairs are small masses of calcium carbonate. It is thought that the pressure which these masses exert upon the hairs leads to afferent impulses which keep us informed of the position of the head when it is at rest. This is then a *static* organ of equilibrium.

SMELL

The true olfactory mucous membrane is very limited in extent, and is confined to that portion of the nasal mucous membrane which covers the medial surface of the superior turbinated bone and the corresponding area of the septum. Here are situated cells which give off the fibers which constitute the olfactory nerve and end in the olfactory bulb. The

air as it is inspired does not pass over this area, but gases and particles of odorous substances which enter the nose reach the olfactory mucous membrane by diffusion. Odorous substances may excite a sensation of smell when introduced into the nostrils in solution in normal saline, but not in distilled water, which probably injures the olfactory cells.

TASTE

Not the whole of the oral mucous membrane is sensitive to sapid substances; the taste organs are confined to the back, the tip, and the edges of the tongue, and to the palate and the pillars of the fauces; their distribution, however, varies considerably in different individuals. The taste-buds, which are found on the sides of the circumvallate papillæ and on the fungiform papillæ, are supposed to serve as end-organs of taste, but probably there are others. The back of the tongue is most sensitive to *bitter* substances; the tip and sides, to *sweet* substances. The other tastes are *acid* and *salt*; flavors are appreciated by the olfactory cells and are not true tastes. Nerve-fibers which are concerned in taste are supplied to the back of the tongue by the glossopharyngeal nerve, and to the anterior two-thirds by the lingual, but the path by which these fibers enter the medulla is uncertain.

MUSCLE SENSE, ETC.

There are certain other sensations which our brain perceives but of which we are not always clearly conscious. These are the sensations which tell us of the position of our limbs, of hunger, thirst, fatigue, and sex. We judge of the position and tension of our muscles and of the position of our joints by means of what is called **muscular sensibility**. The muscles and tissues are also sensitive to deep pressure. The fibers concerned in these sensations are typical posterior root-fibers, some passing up the posterior columns to send impulses to the cerebrum, and others in the tracts of Flechsig

and Gower to the cerebellum. After severe muscular effort this muscle sense is strong enough to produce a distinct sensation, which sensation we call **fatigue**. **Hunger** is probably due to afferent impulses from the gastric mucous membrane, and is accompanied, perhaps caused, by frequent peristaltic contractions of the stomach musculature. **Thirst** seems to be a sensation arising in the pharynx, and probably from a specific end-organ in the mucous membrane. This view is held because of the fact that if thirst were due to drying of the mucosa as by dusty air, merely wetting the pharynx would appease the sensation.

QUESTIONS FOR CHAPTER IV

What are the chief distinctions between internal and external sensation?

Give the application of Weber's law to each of the external sensations.

State the main difference between the sensation of equilibrium from the semicircular canals and that from the utricle and saccule.

Why, when accommodation is relaxed, does a near object appear to be double?

Why is vision indistinct when the eye is immersed in water?

Why do hypermetropic eyes tire more readily than myopic eyes?

What effect on the eye has division of the cervical sympathetic nerve?

When the internal rectus muscle of one eye is paralyzed the eyeball will be rotated outward, owing to the unresisted tonic contraction of the external rectus. Why, under these circumstances, should turning the opposite eye outward cause the injured eye to return to the primary position?

Why does the application of pressure to one side of the eyeball cause diplopia?

If sound-waves reach the retina, why do they not result in visual sensation?

If a man is deprived of sight, how can he properly and successfully adjust himself to his environment?

If a man loses his sight and cutaneous sensibility will he be aware of the position of his body and limbs in space?

Can parallel and divergent rays of light which happen to fall upon the eye be simultaneously focused on the retina?

During accommodation, where are parallel rays brought to a focus?

What sort of lens must be used for the correction of myopia?

What sort of lens is needed after removal of the lens from the eye?

To what extent is vision interfered with by the application of atropin?

How do we know that light does not stimulate the fibers of the optic nerve?

CHAPTER V

BLOOD AND LYMPH

THE blood is an opaque, viscous, alkaline fluid, of an average specific gravity of 1055. The opacity is dependent upon the cells. The viscosity, by which we mean the measure of the stickiness of the blood as it comes in contact with the vessel walls, is increased by a meat diet and decreased by the abundant use of fluids, but is independent of the specific gravity. The opacity of the blood is dependent upon the blood-cells, which are small organized bodies suspended in the fluid, which is called blood-plasma. In man the ratio of blood weight to body weight is about as 1 : 20. The blood-cells form about 50 per cent. by volume of the blood, the remainder being plasma. There are two varieties of blood-cells, red cells, or erythrocytes, and white (colorless) cells, or leukocytes. There are also minute bodies called blood-platelets or plaques.

The functions of the blood are as follows:

(1) It carries to the tissues food-stuffs after they have been properly prepared by the digestive organs.

(2) It carries to the tissues oxygen absorbed from the air in the lungs.

(3) It carries from the tissues various waste products formed in the processes of metabolism.

(4) It is the medium for the transmission of the internal secretions of certain glands.

(5) It aids in equalizing the temperature and water-contents of the body.

(6) It contains substances which neutralize, antagonize, or destroy foreign substances which may be introduced into the organism.

Erythrocytes.—The chemical composition of the red cells is about as follows:

Water.....	61.0 per cent.
Hemoglobin.....	32.0 “
Protein.....	5.6 “
Lecithin and cholesterin.....	0.4 “
Inorganic salts.....	1.0 “

The red cells have no nuclei. They are small biconcave disks of a reddish color. The color is due to hemoglobin, and varies with the degree of oxygenation of this substance from a purple red to a scarlet. There are about 5,000,000 per cubic millimeter of blood, and their function seems to be purely that of carrying oxygen from the lungs to the tissues. This they do by virtue of the contained hemoglobin.

Hemoglobin is a very complex protein body, and may be broken up into a simple protein, *globin*, and a pigment, *hemo-chromogen*, which promptly combines with oxygen to form hematin. Hematin contains all the iron of the hemoglobin molecule, and is a quite stable substance. When this radicle is combined with globin in the proportion of 4 : 90 to form hemoglobin, the compound with oxygen, *oxyhemoglobin*, is a quite unstable body, and is the substance which, formed in the lungs, is carried to the tissues and gives off its oxygen to them. Carbon monoxid can also combine with hemoglobin, but forms a quite stable compound, *carbon monoxid hemoglobin*, which oxygen cannot dissociate.

The means by which hemoglobin is retained in the corpuscle is not clearly understood, but certain abnormal conditions of the plasma result in its escape from the corpuscles and prompt solution in the plasma. The blood becomes darker in color and quite transparent, and is known as *laked blood*; the process is known as **hemolysis**. There are many and varied hemolytic agents: various chemicals, as ether, chloroform, soaps of the higher fatty acids, bile salts, amyl alcohol, saponin, alkalis, snake venom, etc. A decreased osmotic pressure in the plasma results in the corpuscles imbibing water, and if extreme may lead to rupture of the corpuscles,

with setting free of hemoglobin in the plasma. The serum of many animals contains a substance which can hemolyze the corpuscles of another animal. This is not a question of osmotic pressure, but is due to a specific toxic substance called **hemolysin**.

Hemoglobin in its various forms can be recognized in solution by the characteristic bands of shadow which appear in the solar spectrum when the solution is placed before the lens of the spectroscope. *Oxyhemoglobin* causes two bands of shadow: one, narrower and darker, lies at the border of yellow and green, while the other lies toward the blue end of the green; the violet end of the spectrum is also shortened. *Reduced hemoglobin* causes one broad shadow including the yellow and adjacent half of the green, and it also darkens the violet end of the spectrum. *Methemoglobin* results when blood stands for a long time exposed to air. It is an oxygen compound more stable than oxyhemoglobin, and causes a shadow in the blue like that of oxyhemoglobin, and besides this, one from the red-orange region through yellow into green.

There is a *microchemical test* for hemoglobin which depends upon the formation of hemin crystals. Hemin is hematin chlorid, and is produced by warming blood with NaCl and glacial acetic acid under a cover-slip until the acid is evaporated. The crystals are dark-brown rhombic plates and are of microscopic size.

The red blood-cells are a cell without a nucleus, and probably do not have a long life in the blood-stream. There seems to be no place specialized for their destruction, which probably occurs at large in the blood-stream. The bone-marrow normally, and the spleen on special occasions, as after hemorrhage, act as organs for their production.

Leukocytes, or white blood-cells, are composed of about 89 per cent. of water, 9 per cent. of proteins and nucleoproteins, while the remainder is made up of lecithin, cholesterin, fats, and inorganic salts. These cells are colorless, spherical, and contain definite nuclei. Their number varies normally between 5000 and 7000 per cubic millimeter of blood.

The leukocytes possess the power of changing their shape (ameboid movement), and in this way escape through the walls of the capillary blood-vessels (diapedesis) and wander through the tissue spaces; this process is greatly accelerated by the presence of an irritant, the leukocytes collecting in large numbers in an inflamed area, to which they are directed by chemotropism. Leukocytes either ingest bacteria (phagocytosis) or secrete some substance which inhibits their growth and activity. In this way they *afford protection against the inroads of bacteria*. When the blood-stream contains substances which arouse this leukocytic activity, more leukocytes appear in the blood-stream, and their number may rise as high as 50,000 or more per cubic millimeter.

Another function of the leukocytes is to aid in the process of blood coagulation (*q. v.*).

Leukocytes can be divided by morphologic and staining characteristics into various types, which maintain a quite uniform percentage in normal human blood. There are two main classes: cells with a *granular cytoplasm* and cells *without granules*. The cells with granules have a peculiar polymorphic irregularly indented nucleus and arise from the myelocytes of bone-marrow. The majority of these cells have neutrophilic granules and these form 50 to 60 per cent. of all leukocytes (*polymorphonuclear neutrophils*). Others, forming from 2 to 4 per cent., have large eosinophilic granules (*polymorphonuclear eosinophils*), and still others have large basophilic granules (*polymorphonuclear basophils*), and form 0.4 to 2 per cent. of the white cells.

The cells with non-granular cytoplasm are chiefly those formed in the germinal centers of the lymph-glands. There is some evidence in favor of the view that the larger forms of this type are younger immature cells, while the smaller forms are older and mature. Both forms have a deep-staining round nucleus. The *small lymphocytes* form 20 to 30 per cent. of the leukocytes; the *large lymphocytes* form 5 to 10 per cent. There is another type of cell which has been called a *transitional*, because its horseshoe or S-shaped nucleus seems

to be a transition between the round nucleus of the lymphocyte and the polymorphic nucleus of the granular cells. This cell is larger than any other leukocyte and has a non-granular cytoplasm, which may be reticulated. It is probably formed from the endothelial cells of the capillaries and lymph-spaces and forms from 3 to 7 per cent. of the leukocytes. Still another type of cell larger than the granular cells, oval in shape, with a round or oval nucleus, both nucleus and cytoplasm staining deeply, is called a *large mononuclear cell*. Its origin is obscure, but possibly lymphocytic. It may form up to 2 per cent. of the leukocytes in normal blood, but is usually very rare.

Blood-platelets are minute circular or elliptical bodies which occur about 300,000 per cubic millimeter of blood. Their origin is not known, though it is possible they are detached bits of the cytoplasm of the giant cells of the marrow. They disintegrate very readily in shed blood, and play an important part in the process of coagulation (*q. v.*).

Blood-plasma has a chemical composition as follows:

Water.....	90 per cent.
Inorganic Salts (NaCl , Na_2CO_3 , NaHCO_3 , Na_2HPO_4 , NaH_2PO_4 , KCl , K_2SO_4 , $\text{Ca}_3(\text{PO}_4)_2$, CaCl_2 , etc.)..	0.8 per cent.
Dextrose.....	0.12-0.2 per cent.
Fats.....	0.2-(1.0) "
Proteins:	
Serum-albumin.....	4.52 per cent.
Globulins: Serum-globulin.....	3.10 "
Fibrinogen.....	0.50 "
Urea.....	0.02 "
Creatin, uric acid, xanthin bases, lecithin, etc.....	Traces.
Nucleoproteins (?).	
Ferments.	

It will be seen that the plasma contains all the necessary food-stuffs, water, and the inorganic salts, as well as the waste materials, urea, creatin, carbonates, etc. Blood-plasma is alkaline in its reaction to litmus, this being due to the presence of NaHCO_3 , Na_2HPO_4 and combinations of sodium with the protein molecule. These will take up a considerable

amount of acid without changing the reaction, but in acid poisoning further basic radicles are obtained by splitting NH_3 off of protein molecules.

COAGULATION

Coagulation is a very important characteristic of blood which is dependent on the plasma; were it not for this fatal hemorrhage might result from a very trifling wound. In the class of patients known as "bleeders" this is the case; their blood is lacking in the power of clotting. The term *hemophilia* is applied to this condition.

From three to six minutes after human blood leaves the blood-vessel it becomes syrupy in consistence, and later forms a jelly—the **clot**—which contracts and expresses a clear yellow liquid—the **serum**. This change depends upon the appearance in the plasma of innumerable fine fibrils, which are distributed throughout the whole mass of blood in the form of a close meshwork. In the interstices of this the blood-cells are entangled so that they form a part of the clot, though not an indispensable part.

The fibrils, on the formation of which clotting depends, consist of an almost insoluble protein which is called **fibrin**. If the blood, as it is shed, be collected in a vessel and whipped with a bundle of twigs, the fibrin fibrils adhere as fast as they are formed to the whipper, and may thus be removed from the blood. The blood thus **defibrinated** remains liquid indefinitely, the clot having been removed, and, by its appearance, cannot be distinguished from normal blood. If the fibrin collected in this way be washed free from the few blood-cells which are held between its fibrils, it is found to be a stringy, elastic substance, gray in color.

In composition, serum is similar to plasma, save that it contains no fibrinogen; in addition, it contains a ferment-like substance of which mention will be made below. We see, then, that fibrinogen disappears during the clotting of blood. Further, if fibrinogen be removed before the blood has had

time to clot, clotting will be entirely prevented; thus fibrinogen is necessary to the clotting of blood.

The **clotting of blood** depends upon the conversion of fibrinogen into fibrin. The next question is, What is the cause of this conversion? The clotting of blood may be prevented by the addition of a certain quantity of a salt, such as magnesium sulphate, the amount added being insufficient to precipitate the proteins of the plasma. Blood so treated is known as *salted blood*, and from it, by allowing the blood-cells to settle, can be obtained salted plasma, which remains liquid. Now, if to salted plasma there be added a small quantity of blood-serum, or a small quantity of an extract made from a blood-clot, the salted plasma clots; its fibrinogen is converted into fibrin. The small quantity of serum which is necessary indicates that the process may depend upon the action of a ferment or enzyme. Clotting is retarded by cold and accelerated by moderate warming. These facts have been used as evidence that clotting is caused by an enzyme, which enzyme is called **thrombin** or **fibrin ferment**. Thrombin is considered to be formed by the union of three factors: *thrombogen* or *prothrombin*, normally present in the plasma; *calcium*, in the plasma as an inorganic salt; and *thrombokinase*, a hypothetical thromboplastic substance, formed by the disintegration of tissue and blood-cells which results with hemorrhage. Thrombokinase is formed chiefly by the blood-plates, which on contact with any foreign substance disintegrate and set this substance free. The kinase joins with calcium and thrombogen to form thrombin, and this converts fibrinogen to fibrin and forms the clot.

Blood does not clot in the vessels because there is not enough thrombokinase present at a given time. An anti-thrombin may exist which tends to check the action of any thrombin that may be formed.

A more recent theory of coagulation denies that thrombin is a ferment because of the fact that *it may be boiled* under proper precautions and still remain active, and that if a minimal amount of thrombin be added to fibrinogen the latter

will not all be changed to fibrin, but if more thrombin be added, more fibrin will be formed. Prothrombin is supposed to exist in the blood and to be capable of combining with calcium to form thrombin. Antithrombin exists in sufficient amount to check the thrombin action. A thromboplastic substance (kinase) is formed by disintegration of tissue cells and blood-plates which unites with the antithrombin and inactivates it, so that thrombin is free to unite with fibrinogen in a sort of physicochemical combination to form fibrin.

Blood will not clot in a section of a vessel tied off *in situ*, for there is no destruction of tissue cells and no kinase is formed. Kinase is formed but slowly if blood comes in contact only with oiled or paraffined surfaces. Blood will not clot if the calcium is precipitated by oxalate solutions, or if the thrombin action is inhibited by cooling or by solutions of neutral salts like magnesium sulphate. Certain other substances restrain the thrombin action and prevent clotting; snake venom, peptone, trypsin, and pepsin increase the antithrombin, while hirudin (leech extract) seems to contain antithrombin. Heat and increasing the surface of contact both hasten clotting.

Transfusion.—After severe hemorrhage it is sometimes necessary to increase the bulk of the patient's blood by the injection of some liquid, and the choice of this liquid is important. Since defibrinated blood always contains fibrin-ferment, it is inadvisable to inject the blood of another person, even if that person is known to be perfectly healthy and the blood has been whipped to prevent its coagulation; the fibrin-ferment contained in it may cause intravascular clotting of the remnant of the patient's own blood. The injection of blood taken from some other animal is objectionable for the same reason, and possesses another disadvantage—the possibility of hemolysis.

The direct transfusion of blood from the vessel of one person (the donor) into the vessel of another person (the recipient), although considered dangerous until recently, is now a practicable and safe procedure if appropriate facilities and skill are

available. What amounts to a direct anastomosis either with or without a tube to connect the vessels has been used successfully in cases of severe hemorrhage, the tube being always paraffined to decrease the production of kinase. If care is taken to do it so quickly that there is no tendency to clot, the blood may be drawn up through an oiled needle into an oiled syringe and quickly injected into the vein of the recipient.

In spite of the increasing availability of direct transfusion of human blood, recourse must be had, in most instances, to infusions of solutions of inorganic salts, given subcutaneously or intravenously. A fluid for such purposes should be a perfect solution, isotonic with the blood; *i. e.*, the equivalent of an 0.85 per cent. solution of sodium chlorid, sterile and heated to body temperature.

Calcium, potassium, and sodium salts should be used in about the following proportions to have an infusion fluid of most efficiency: Calcium chlorid, 0.026 per cent.; potassium chlorid, 0.035 per cent.; sodium chlorid, 0.75 per cent.

After hemorrhage an infusion of a saline solution promptly fills the place of the bulk of blood-plasma lost, and the regeneration of red blood-cells follows at a slower rate, so that they may not be in normal number of days or weeks.

DEFENSIVE ACTION OF BLOOD

Clotting, of course, protects the body against hemorrhage, but the blood has a still more important function to protect the body against disease. The **leukocytes** attack and destroy any foreign substance with which they can come in contact, but the defensive power of the plasma is more remarkable. The plasma contains several different chemical substances which each have special protective functions. **Hemolysins**, already mentioned, are soluble proteins, which are destroyed by heating to 55° C. They can be produced in any animal, if not already present, by repeated injections of blood-corpuscles of another species. This process is called *immuniza-*

tion and the serum an *immune serum*. The hemolysin produced is specific for the corpuscles of the species from which the corpuscles were obtained for injection. If a protein poison, a toxin, is injected, **antitoxin** is formed, which will combine with the toxin and render it harmless. **Bacteriolysins** are similar substances produced by the action of bacteria in the blood-stream, which tend to dissolve and destroy them. These are also specific for the bacterial species. **Agglutinins** are bodies which cause bacteria to clump together and to become immobile. They are present in all plasma, but can be increased by repeated injections of the bacteria. They also are specific. **Precipitins** are also protein bodies; they cause the precipitation of any foreign protein which may be brought into the plasma. These can also be increased by repeated injection and are specific. If serum is taken from a rabbit which has been immunized to human serum, it will form a precipitate with human serum, and with the serum of no other animal except that of anthropoid apes. This is the so-called biologic test for suspected blood.

Detection of Blood and the Identification of Its Source.—If blood has been recently shed, microscopic examination of the specimen diluted with salt solution will suffice to determine its origin by recognition of the red blood-cells. If blood has been shed some time previous to the examination, it can be detected by spectroscopic analysis or by the presence of hemin crystals, or by the biologic test, as described above.

THE LYMPH

Lymph is formed by the filtration of plasma through the walls of the capillaries into the lymph-spaces, which lie outside the capillaries and between the cells of the various tissues. Its composition is, however, not precisely the same as that of the plasma, owing to the fact that the proteins do not pass through the capillary wall as readily as do the other constituents of the plasma. The capillaries of different parts of the body differ in their permeability, those of the liver being the

most permeable, those of the lower limbs the least so; consequently, the lymph formed in different parts differs in composition; that formed in the liver may contain proteins to the extent of 6 per cent.; that formed in the legs, about 3 per cent.

The force concerned in causing the filtration of the plasma into the lymph-spaces—in other words, in the formation of the lymph—is the intracapillary blood-pressure. To this force are opposed the following: the slight resistance offered by the capillary wall to the passage through it of water and inorganic salts; the much more effective resistance which is opposed to the passage of proteins; and the osmotic pressure which is exerted by that portion of the proteins which does not pass through the wall, but remains within the capillaries. This portion is usually the larger. Proteins form about 8 per cent. of the plasma, and exert an osmotic pressure of about 30 mm. of mercury; the lymph contains about 3 per cent. proteins, with an osmotic pressure of 10 mm. of mercury or a little more, exerted in the opposite direction; so that the balance of osmotic pressure which is effective in resisting the outward passage of lymph amounts to about 20 mm. Hg. The intracapillary blood-pressure is, under ordinary circumstances, from 30 to 50 mm. Hg, and suffices to overcome the opposing forces which have been mentioned above; but if for any reason—*e. g.*, after severe hemorrhage—the intracapillary pressure falls below 20 mm. Hg, the effective balance of osmotic pressure due to the predominance of proteins within the capillaries will cause the absorption of water from the lymph-spaces.

That portion of the lymphatic system concerned in the absorption of fat from the intestine, and the conveying of the lymph and its contained emulsified and saponified fats by the lacteals, the receptaculum chyli, and the thoracic duct, to the blood-stream, illustrates best the various factors which control the flow of lymph in various parts of the body. They may be summed up as follows:

1. Intracapillary pressure.

2. Force of diffusion depending upon the inequality in the chemical composition of the blood-plasma and the liquid

outside of the capillaries, or between this liquid and the contents of the tissue elements.

3. The force of osmotic pressure.
4. The valves in the lymph-vessels.
5. The effect of contraction and relaxation of the skeletal and visceral musculature.
6. The negative pressure in the thorax acting upon the surface of the thoracic duct.
7. The negative pressure in the great veins at the base of the neck acting upon the opening of the thoracic duct at its venous junction.

SPLEEN AND LYMPH-NODES

We know but little of the function of the spleen and lymph-nodes, but they seem to be in some way analogous. Removal of the spleen leads to an increased excretion of iron for a time, and this is accompanied by a decrease in the red blood-cells and in hemoglobin. After a time the blood returns to normal, and this is accompanied by an increase in the size of the lymph-nodes, especially the hemolymph-nodes. Injection of splenic extract, moreover, leads to an increase in the number of red cells in the blood.

It seems as though we could conclude that the spleen has to do with the retention and preservation of iron from the hemoglobin of destroyed red blood-cells, so that the iron might be used over again, and likewise that the spleen furnishes a hormone which stimulates the bone-marrow to a more rapid production of red cells. Both of these functions can be taken over by the lymph-nodes, if necessary.

The lymph-nodes have, however, a quite special function, which is to stop the passage of any bacteria which may gain entrance to the lymph-channels and to prevent their entrance into the blood.

It has been stated previously that certain of the leukocytes are formed in the lymph-nodes, perhaps their most important function.

QUESTIONS FOR CHAPTER V

What proportion of a blood-clot consists of fibrin?

How does hemoglobin differ from other proteins?

Give the functions of the blood as a whole, and of the red cells and leukocytes independently.

What are some of the changes which occur in blood when it is boiled?

What are the effects of removing all the inorganic salts from blood?

Does the "salting" of blood prevent the formation of fibrin-ferment or does it prevent its activity?

Does the addition of fibrin-ferment to defibrinated blood cause it to clot?

How may defibrinated blood be caused to clot?

If the coagulation of blood be prevented by rapidly cooling it to 0° C., and keeping it at this temperature until most of the cells have settled, and if the upper and lower layers of plasma be separated and warmed, which will coagulate first?

By what different methods may fibrinogen be removed from the blood without at the same time removing the other proteins?

What effect has the addition of defibrinated blood on a solution of pure fibrinogen?

What is the effect of introducing a foreign body into the blood-vessels?

What are the agencies which may be brought into activity to resist the harmful effect of foreign substances in the blood-stream?

Why does the dilution of salted blood cause it to clot?

Why does packing a wound with gauze hasten clotting?

Is lymph a product of the lymphatic glands?

What is the difference between lymph and serum?

What are the important constituents of lymph?

Why does serum remain liquid at 0° C.?

How may the osmotic pressure of plasma be reduced?

Why should distilled water not be injected into the blood-vessels?

How much blood does the body of a man contain if his weight is 150 pounds?

Give the origin of the red and white blood-cells.

What is best to do for an animal which has lost a large amount of blood?

Is the flow of lymph dependent upon the force of the heart-beat?

How could suspected blood be identified?

CHAPTER VI

RESPIRATION

THE function of the lungs consists in the exposure of the blood to the air, in order that an exchange of gases may take place between them. The air in the alveoli in whose walls the exchange takes place must be renewed; the lungs must be ventilated. This is accomplished by the respiratory muscles, which by their contraction bring about a variation in the capacity of the thorax and consequently in that of the lungs. The inner surface of the lung and the outer surface of the thorax are both exposed to the atmospheric pressure; the two are thus held closely in contact with one another by a pressure of 14 pounds to the square inch, and every movement of the chest wall must be accompanied by a similar expansion or diminution of the lung. An enlargement of the thorax will, therefore, by increasing the capacity of the lungs, lower the pressure within them, and, if the glottis be open, lead to the entrance of air.

The muscles which may assist in the enlargement of the thoracic cavity and lungs, and thus act as **muscles of inspiration**, are the diaphragm, which on contraction increases the vertical diameter of the chest, and the scaleni, levatores costarum, serrati postici superiores, sternocleidomastoids, external intercostals, and intercartilaginous portion of the internal intercostals, which all take part in raising the ribs. This increases the lateral and anteroposterior diameters of the chest, owing to the obliquity of the costovertebral hinge. Quiet **expiration** is accomplished, without the aid of muscular contraction, by the elastic recoil of parts which are distorted during inspiration, such as the costal cartilages, the abdominal wall, and the lungs, and by the weight of the ribs, sternum, thoracic muscles, etc. In forced expiration the diaphragm is pushed upward by the abdominal viscera through the con-

traction of the abdominal muscles, while the ribs are drawn downward by the contraction of the triangulares sterni, interosseous portion of the internal intercostals, etc.

Even when the inspiratory muscles are at rest, there exists, between the layers of the pleuræ a **negative pressure**; that is, a pressure less than atmospheric pressure. This is due to the fact that a certain amount of the atmospheric pressure is consumed in holding the lung in contact with the inner surface of the thorax and the outer surface of the heart and vessels. The lungs are not large enough to fill the thoracic cavity unless they are inflated, and their inflation requires a small amount of force. If the interpleural pressure be measured when the respiratory muscles are quiescent, or after death, it will be found to be about 754 mm. of mercury, or about 6 mm. Hg less than atmospheric pressure; a negative pressure, then, of 6 mm. Hg. At the end of a forcible inspiration the interpleural pressure may fall as low as 730 mm. Hg, for the lungs are further inflated and, of course, offer more resistance to the inflating force—the atmospheric pressure. The interpleural pressure during forcible expiration may rise above atmospheric pressure, but is always lower than the pressure within the alveoli.

If the chest wall be pierced, so that air can enter the interpleural space, the outer as well as the inner surface of the lung being now exposed to the full atmospheric pressure, the lung, owing to its own elasticity, will promptly collapse. If both sides of the thorax be perforated, ventilation must cease, for since the elasticity of the lungs will resist the entrance of air through the trachea into themselves an enlargement of the chest will only result in the entrance of air into the interpleural spaces.

The importance of the interpleural negative pressure, in respect to the flow of blood through the veins into the chest, will be further mentioned when considering the circulation. The outer surface of the heart and large intrathoracic vessels is subjected, when the thorax is at rest, to a pressure of only 754 mm. Hg, while the veins which lie outside the chest are

exposed to the full atmospheric pressure—760 mm. Hg; it is evident, then, that blood will be forced from points where the veins are more to a point where they are less compressed. Inspiration will further this tendency; expiration will lessen it, and, if forcible, will obstruct the entrance of blood because, as has been said, the interpleural pressure may become positive.

Respiration may seem to assume one of two types, diaphragmatic or costal, but under normal conditions of body movements both the diaphragm and the thoracic muscles enter into every respiratory movement. Position of the body, clothing, or habit may modify the normal freedom of respiratory movement, and it is seen that women usually breathe more costally than diaphragmatically, and that the reverse is true with men.

In quiet breathing the chest is neither expanded nor contracted to the full extent possible, so that the ventilation of the lungs is not so complete as might be. The amount of air ordinarily inspired and expired is about 500 c.c., and is known as the **tidal air**; in addition to this, an amount which varies with the capacity of the chest, and is called the **complemental air**, can be inspired, the average quantity being in the neighborhood of 1500 c.c. After the expiration of the tidal air about 1500 c.c. more may be expelled, this volume being known as the **reserve**, or **supplemental air**. These three volumes taken together, and amounting to 3500 c.c., are called the **respiratory**, or **vital, capacity**. Not all the air can be expelled from the lungs; there remains after the most forcible expiration about 1000 c.c.—the **residual air**.

The division of the cavity of the lungs into innumerable small alveoli enormously increases the respiratory surface, which is estimated as being 90 square meters.

On its way through the upper air-passages the temperature of the inspired air is raised or lowered to that of the body; it is moistened, unless already saturated with water, and, to a certain extent, purified from particles of foreign matter which adhere to the moist mucous membrane, and are carried toward the mouth and nose by the movements of the cilia.

Respiration may be divided into external respiration, the exchange of gases between the air and the blood which occurs in the lungs; and internal respiration, the exchange of gases which takes place between the blood and lymph and the tissues.

External Respiration.—Diffusion goes on rapidly between the alveolar air and the tidal air that is inspired, the latter losing oxygen to the extent of about 6 per cent. by volume, and gaining about 5 per cent. by volume of carbon dioxid.

The exchange of gases which occurs between the air in the pulmonary alveoli and the blood in the capillaries of the lung is, perhaps, not to be wholly explained by diffusion, some observers having found the tension of oxygen to be greater in arterial blood than in the alveoli of the lungs; this is the opposite of what we should expect as the result of simple diffusion. A specific secretory activity has been claimed for the lining cells of the alveoli, but we may assume that diffusion is the main factor, and perhaps the only one.

Oxygen occurs in the blood in simple solution in the plasma, but chiefly in a loose chemical combination with the hemoglobin. If the blood is subjected to a low partial pressure of oxygen as it is in the tissues, the oxygen is given off very rapidly. It forms 12 per cent. of venous blood by volume, and 19 per cent. of arterial. Carbon dioxid occurs in simple solution in the plasma, and also in a loose chemical combination with hemoglobin, and a firmer one with the blood alkali as carbonate or bicarbonate. The splitting of these carbonates to free the CO_2 is brought about by the oxyhemoglobin, which acts as a weak acid. CO_2 forms 40 per cent. by volume of arterial blood and 47 per cent. of venous. It will be noticed that only a small proportion of the carbon dioxid is eliminated as the blood passes through the lungs, and that only about half the oxygen disappears from the arterial blood on its passage from the arterioles to the veins through the systemic capillaries.

Internal Respiration.—The cells of the various tissues prevent the accumulation of oxygen in the lymph which sur-

rounds them; they display a great avidity for oxygen and take it up as fast as it reaches them, thus maintaining in the lymph a practical oxygen vacuum. Consequently, a rapid diffusion of oxygen must occur through the capillary wall from the plasma to the lymph; and as the partial pressure of oxygen diminishes in the plasma, the oxyhemoglobin of the red cells must, to a certain extent, be reduced. Oxygen will pass from the blood-cells to the plasma, and from the plasma into the lymph, thus reaching the tissue cells. The individual capillaries are, however, so short that each red cell remains in this district but a brief period, and time is not given for the reduction of all its oxyhemoglobin; still more is this the case when the arterioles of an active organ are dilated, and the blood flows through its capillaries with increased celerity. Under these circumstances a larger number of red cells will pass through each capillary in a given time, and though in the aggregate more oxygen will be given up to the lymph, each cell will part with a smaller quantity than usual, and the blood reaching the veins will retain its arterial color.

The oxygen passes from the hemoglobin to the lymph and in solution in this it comes in contact with the tissues. The carbon dioxid passes from the cells to the lymph, and thus reaches the blood-plasma.

REGULATION OF RESPIRATORY RATE

The respiratory muscles are under the control of the respiratory center which is situated in the spinal bulb; in the neighborhood, therefore, of the important centers which govern the circulation. The respiratory center is bilateral, but the two halves, connected by commissural fibers, act in unison. It is **rhythmically active**, ordinarily at the rate of from fifteen to twenty respirations per minute, the respiratory rhythm usually varying with the heart rhythm as one to four. This center is exceedingly sensitive to nerve impulses which reach it from the periphery or from the higher centers in the brain, and to changes in the chemical composition of the blood. The nerve-fibers emanating from the respiratory

center pass downward into the spinal cord. They decussate in part, and end in the gray matter of the cord in the neighborhood of the motor nerve-cells, which, situated in the different regions of the cord, innervate the respiratory muscles. The center also dispatches impulses to the nuclei of some of the motor cranial nerves, and thus governs accessory respiratory movements which accompany inspiration, such as those of the vocal cords and *alæ nasi*.

Destruction of the center puts an end to respiration and proves fatal. Division of the spinal cord just below the origin of the phrenic nerve causes paralysis of the thoracic and abdominal muscles concerned in respiration, but the diaphragm, innervated through the phrenic nerve, remains active. Division of the cord above the origin of the phrenic nerve proves as fatal as destruction of the respiratory center, though life may be supported for half an hour or so by the contractions of the sternocleidomastoids, innervated through the spinal accessory nerve.

Of the various stimuli to which the center is responsive, the condition of the blood is the most important. A **venous condition of the blood** acts as a strong stimulus to the respiratory center; consequently, it is impossible to voluntarily cease breathing for long at a time. It is easy to inhibit the center and prevent its response up to a certain point, but as the blood becomes more and more venous the stimulation of the center grows so forcible that it overcomes our most strenuous efforts at inhibition, and we begin to breathe in spite of ourselves.

It seems to become increasingly certain that it is the increase in CO_2 more than the decrease in oxygen which forms the normal stimulus to the respiratory center and causes its rhythmic activity. The center responds to this chemical stimulus even when isolated from all afferent nerve impulses, and is, therefore, considered to be spontaneously active. An increased acidity of the blood increases the activity of the center and likewise an increase in the temperature.

The respiratory center may be stimulated through almost

any afferent nerve, as, for example, a dash of cold water, the will, emotional states, etc. The most important afferent nerves are those of the respiratory tract itself. Division of both vagi results in a slowed respiration of increased depth.

If the lung is suddenly aspirated, with the vagi intact, there results a contraction of the diaphragm; if the lung is suddenly inflated, the diaphragm relaxes and a forced expiration ensues. This, together with the fact that stimulation of the central end of the cut vagus abolishes the slowing of respiration, is taken to mean that the vagus contains two sets of afferent fibers. One set, stimulated by respiration, inhibits inspiration; the other set, stimulated by expiration, stimulates inspiration. Normal breathing is thus a balance at an accelerated rate and less deep than it would otherwise be.

The **inferior or recurrent laryngeal nerves** are pure motor nerves to the muscles of the larynx. The **superior laryngeal nerves** are motor for the cricothyroid muscle and sensory for the mucous membrane of the glottis and the larynx. Stimulation of the superior laryngeal nerves or of the mucous membrane in their distribution results in a cessation of inspiration, followed, as a rule, by an expiratory effort, thus imitating the chain of events following the presence of an irritating gas or foreign substance at the entrance of the larynx, *i. e.*, holding the breath and then *coughing*. Coughing may also result from irritation of the afferent fibers of the vagus in the lungs.

During swallowing respiration is stopped by inhibition of the respiratory center through the glossopharyngeal nerve, the pharyngeal terminations of which are stimulated by the substance swallowed, thus affording a mechanism which prevents the inhalation of food into the trachea. The center may also be inhibited on the introduction of irritating gases or liquids into the nasal fossæ, the terminations of the fifth cranial nerve being thus stimulated; this results in *sneezing*, which is much like coughing except that part of the air is expelled through the nose.

When the proper arterialization of the blood is prevented, **hyperpnea**, or increased depth and frequency of respiration,

ensues; if this does not result in the access of oxygen to the required extent, or in the removal of the surplus carbon dioxide, or both, there follows more exaggerated breathing, **dyspnea**. These two terms differ only as to degree, and the causal conditions vary greatly; stimulation of afferent nerves, increased vensity of the blood, the acid products of muscular work or of perverted metabolism which may occur in the blood, decreased blood flow through the center due to hemorrhage or failing circulation, obstruction in the respiratory passages, these form only an incomplete list. To advanced stages of dyspnea the term **asphyxia** is given, which describes a series of phenomena beginning with deep forced inspirations and continuing until general convulsions, exhaustion, and death supervene.

Apnea, or temporary cessation of breathing, may be induced by rapid forced respiration; this, in the normal animal, is not due entirely to overaëration of the blood, for the blood will take up little more oxygen than usual when pure oxygen is breathed, and the same condition is produced if hydrogen be used for inflating the lungs. It is caused partly by the effect produced on the respiratory center through the afferent fibers of the vagus, the pulmonary terminations of which are stimulated by the rapidly repeated distention and collapse of the lungs. If both vagi have previously been divided, it is more difficult to induce apnea, and impossible by the use of hydrogen, so that both factors are probably operative.

QUESTIONS FOR CHAPTER VI

If a U-tube manometer is connected with a cannula which is thrust through the chest wall, which limb of the U will be the higher?

Why are the lungs less well protected after division of the glossopharyngeal nerves?

Why is it dangerous to divide the laryngeal nerves?

Curari paralyzes the skeletal muscles. How does it cause death?

Why is paralysis of the expiratory less injurious than that of the inspiratory muscles?

Why is ventilation necessary?

How does the contraction of the bronchial muscles affect respiration?

How could it be proved that the respiratory center is automatically active?

How is this automatic activity regulated?

CHAPTER VII

THE CIRCULATION OF THE BLOOD

THE term "circulation" signifies that the blood follows a path which finally returns into itself; it moves in its path always in a definite direction and never in the reverse. This is made possible by the presence of the valves of the veins, which prevent any movement of blood toward the periphery, and the arrangement of the valves in the heart, which allow the blood to pass in one direction, but permit of no return.

In the human **fetus** the blood from the mother enters the child's body by the umbilical vein from the placenta. The umbilical vein carries the blood to the liver, where, as the ductus venosus, it connects with the portal vein, and thence to the inferior vena cava, which carries the blood to the right auricle, the foramen ovale permitting direct connection with the left auricle. From the left auricle the blood passes through the mitral valve to the left ventricle, whence it goes to the aorta, past the aortic semilunar valve, and is distributed to the tissues of the body, but chiefly to the head and upper extremities. It returns to the superior vena cava and thence to the right auricle and through the tricuspid valve to the right ventricle, and past the pulmonary semilunar valve to the pulmonary artery, from which most of the blood passes directly to the descending aorta through the ductus arteriosus. The greater part of this blood goes then to the hypogastric arteries, which are continuous with the umbilical arteries, and thence to the placenta.

In the human **adult** the blood from the superior and inferior venæ cavæ enters the right auricle, whence it passes through the tricuspid valve to the right ventricle. From the right ventricle the blood is forced past the pulmonary semilunar

valve to the pulmonary artery, to the pulmonary capillaries, and back through the pulmonary veins to the left auricle. From the left auricle the blood passes through the mitral valve to the left ventricle, whence it is forced past the aortic semi-lunar valve into the aorta and its branches. The blood that passes to the organs of digestion is collected by the tributaries of the portal vein, and is again distributed by the branches of the portal vein to the parenchyma of the liver, from which it is again collected and enters the inferior vena cava, all the rest of the blood from the tissues of the body being collected directly from the capillaries by the tributaries of the superior and inferior venæ cavæ.

The path of the flow is thus seen to be essentially a continuous tube with variations in its caliber, and specialized at one point to form a contracting organ. The rhythmic contractility of the heart and the distensibility and elastic recoil of the walls of the aorta and large arteries cause the movement of the blood, the continuous movement in the same direction being determined by the position and attachments of the valves at various points.

The Heart Cycle.—The heart-beat is normally the result of an impulse which arises in the *sino-auricular node* (Keith-Flack node)—a collection of tissue representing a remnant of the sinus venosus of the lower vertebrates. It lies in the sulcus terminalis beginning just below the angle formed by the junction of the superior vena cava with the upper surface of the right auricular appendix. The contraction spreads to, and sweeps over, the *auricular musculature*, driving the contents of the auricles into the ventricles, and constituting the auricular systole. This merely completes the filling of the ventricle, in which, previous to the systole of the auricle, blood has accumulated by inflow, through the latter, from the veins.

As the ventricles fill, the free edges of the auriculoventricular valves are carried upward and approach one another, their complete closure being effected by the more abrupt rise of pressure within the ventricles produced by the auricular

systole, thus arranging that at the beginning of ventricular systole these valves shall be already closed.

The auricular systole lasts but 0.1 second, and is followed by relaxation or diastole. Were it not for the auricles, the flow of blood from the veins into the heart would be checked during the ventricular systole which now ensues; as it is, the auricles not only assist in the filling of the ventricles, but constitute a time-saving reservoir which is of special value when the heart rhythm is rapid.

The ventricular systole does not begin until from 0.12 to 0.20 second after the beginning of that of the auricle. During this time the contraction sweeps over the auricular muscle in a wave-like manner and produces an effect upon the *auriculoventricular node* (node of Tawara), which results in the passage of an impulse, possibly also a contraction, along the *bundle of His* and its *arborizations*. The terminal branches of this bundle lie about the bases of the papillary muscles of each ventricle, and spread out in a network beneath the endocardium. The impulse passing along the bundle branches thus reaches both ventricles almost simultaneously, so that they both contract at the same time.

The contraction of the ventricular muscle shortens the long diameter of the heart and decreases its circumference. The apex is thrust against the chest wall by this change in shape, causing the apex impulse which we feel in the fourth left intercostal space. The change in size results in a rise in the pressure within the ventricles. (See Fig. 26.)

Intraventricular pressure rises rapidly as the systole proceeds, the back-flow of blood into the auricles being prevented by the tricuspid and mitral valves, which are held in place by their tendinous cords attached to the papillary muscles. The outflow into the arteries is, for the moment, prevented because the semilunar valves are kept closed by the higher pressures in the pulmonary artery and aorta.

As soon, however, as the pressure within the ventricle rises, in the one case, higher than that in the pulmonary artery, in the other, above that in the aorta, the semilunar valves

must open and the blood be ejected by the ventricles into the arteries. The ventricles probably never completely empty themselves. Now follows the ventricular diastole, or period of relaxation and rest, at the beginning of which the pressure within the ventricle falls below that in the aorta, so that the semilunar valves close. A short interval elapses before the

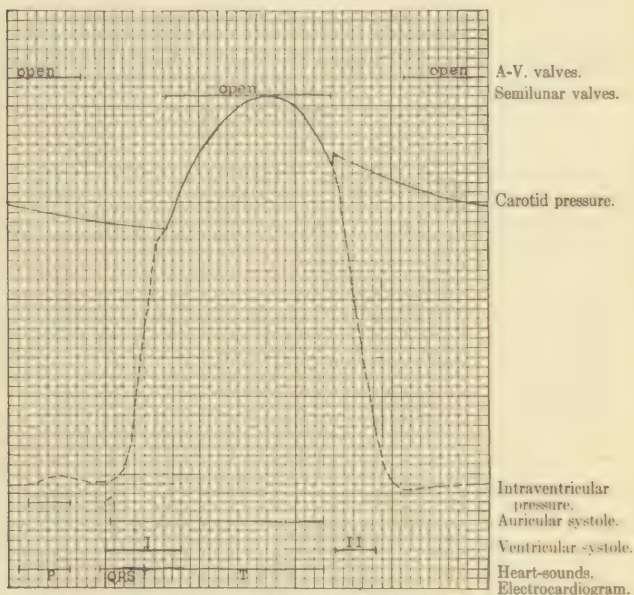


Fig. 26.—Pressure and time relations during the cardiac cycle. 1 division absc. = .02 sec. 1 division ord. = 4 mm. mercury.

intraventricular pressure falls below that within the auricle, and until this point is reached the auriculoventricular valves must, of course, remain closed. The whole series of events just described occurs simultaneously in the right and left hearts, and constitutes a heart cycle.

It will be noticed in Fig. 26, where the heart rate is represented as being 60 per minute, that while the auricular sys-

tole lasts 0.1 second and the diastole 0.9, the systole of the ventricle occupies 0.45 and its diastole 0.55 second, the ventricular cycle beginning 0.17 second later than that of the auricle. When the frequency of the heart-beat is increased each cycle is, of course, shortened, this reduction being accomplished, for the most part, at the expense of the diastole, the systole of the ventricle lasting almost as long as usual.

The **behavior of the valves** depends upon the relative height of the pressure on either side of them (Fig. 26); the auriculo-ventricular valves, for instance, remain closed as long as the pressure within the ventricle is higher than that in the auricle; when the pressure within the ventricle falls below that in the auricle they open, and remain so until the intra-ventricular pressure again predominates. In the same way, the semilunar valves are kept closed by an arterial pressure that is greater than the intraventricular pressure, and give way when the ventricular rises above the arterial. It will be noticed that both sets of valves are, for two short periods, closed at the same time.

The auriculoventricular valves, the tricuspid and mitral, depend upon the fibrous bands, the chordæ tendineæ and their attachment to the papillary muscles, to prevent their being forced through the auricles on ventricular systole. The aortic and pulmonary semilunar valves depend upon the cup-shaped attachment of their cusps to prevent inversion during ventricular diastole.

The function of the papillary muscles is to contract during ventricular systole, pull upon the chordæ tendineæ, and thereby give extra support to the cusps of the auriculo-ventricular valves when they are subject to the greatest strain. The fact that each muscle sends chordæ to two adjacent flaps also tends to hold the valve edges together.

Electric Phenomena.—The contraction of the heart muscle, like that of skeletal muscle, is accompanied by a production of electricity. We can lead off this current from two points of the heart or from any two points on the surface of the body,

since the current flows readily through the tissues. The arms and left leg are usually used. A record of the electric variations obtained by a galvanometer is called an *electrocardiogram*, and shows three main waves or peaks (Fig. 26). The first wave is a small rounded elevation due to the activity of the auricular muscle, and is usually called the P wave. This is followed after the auriculoventricular interval of 0.12–0.20 second by a series of sharp upward and downward peaks occupying about 0.08 second, and then a slow rounded or peaked elevation which lasts till the end of the systolic period. These are all due to the activity of the ventricular muscle. The principal peak of the first group is normally directed upward and is called the R wave; the last slow elevation is called the T wave. The electrocardiogram varies with the site of the leading-off electrodes with the position of the heart, but most of all with the condition and mode of contraction of the cardiac muscle.

Rate Regulation.—The **rate** at which the heart beats is governed by the central nervous system, which, in this respect, exerts its control chiefly over the sino-auricular node, the sinus rhythm setting the pace for auricles and ventricles as described. If the auricles are caused to stop beating by the stimulation of the pneumogastric nerve, the ventricles, after a brief pause, begin to beat with a much slower rhythm of their own, some point within them, probably in the bundle of Hiss, taking over the stimulus production.

Although the central nervous system controls the rate of the heart-beat, it is by no means essential to its continuance, as may be shown by removing the heart from the body, when, if properly supplied with oxygenated blood, it may go on beating for hours. The cardiac muscle itself possesses an inherent power of rhythmic contraction, for even small isolated pieces of the ventricle which contain no nerve-cells will beat rhythmically if supplied with arterial blood.

Heart-sounds.—If the ear be placed against the chest wall, two sounds are heard each time the heart beats. The first accompanies the ventricular systole, and is more pro-

longed than the second, which is early diastolic (see Fig. 26). The **first sound**, which seems to be compound, is probably produced in part by the contraction of the muscle of the ventricle, and in part by the vibration of the auriculoventricular valves on closure. Each ventricle takes part in the production of the first sound. The **second sound** occurs very soon after the beginning of the ventricular diastole, and is due to the vibration of the semilunar valves at or just after their closure.

If the **rate of blood flow** through vessels of different size be compared, it will be seen that the larger the vessel, the greater the speed. In the aorta the blood flows most rapidly, for the sectional area of this vessel is smaller than the united sectional area of its branches, consequently the blood, having less room, must flow more quickly. The rate of flow is inversely proportional to the *width of bed*. The united sectional area of the systemic capillaries has been estimated to be as much as 800 times that of the aorta; in this district, then, the stream is sluggish. As the blood flows from the capillaries into the small veins, the width of bed decreases and the stream quickens; in large veins the rate will approach, but never equal, that in the aorta. The velocity of the circulation as a whole, of course, increases or decreases with a change in the rate and strength of the heart-beat.

The speed of the blood is greatest in the arteries nearest the heart, diminishing gradually until, in the capillaries, the rate is only 0.5 mm. per second. From the capillaries the speed of blood flow increases gradually as the veins approach the heart, where it is again rapid. It has been computed that the average time for a given corpuscle to make a complete circuit would be 23 seconds in man, though this, of course, varies whether a short or a long circuit is taken.

BLOOD-PRESSURE

The blood as it flows through the vessels is under constant pressure. This pressure is the product of the propelling

force exerted by the heart and the resistance offered to the flow by hydraulic friction. During the diastole of the ventricle the flow is kept up by the elastic and overfilled aorta and larger arteries. As liquid flows through a tube, friction exists between its particles; and the nearer the wall of the tube, the greater the friction; therefore, if we compare the flow of liquid through a large tube with its flow through a number of small tubes, the united sectional area of which is equal to the sectional area of the large tube, we shall find that it meets with much more resistance in the small ones; for a much larger proportion of the liquid will flow in the neighborhood of the tube wall and the friction will be greater. The blood, then, will meet with most resistance on passing through the innumerable arterioles and capillaries into which the larger arteries divide; this is usually spoken of as the **peripheral resistance**. The overcoming of this peripheral resistance uses up most of the heart force, and by the time the blood reaches the veins it flows under but little pressure, which, however, suffices to carry it as far as the right heart. The fall in pressure is continuous from the beginning of the aorta to the ending of the veins, for friction comes into play along the whole route. In the arteries the fall is a gradual one, but it becomes abrupt in the arteriole and capillary district, while in the veins the pressure again decreases slowly.

The blood-pressure is variable, especially that in the arteries. As there are two factors in the production of the blood-pressure, so there are two main causes concerned in bringing about its variation; namely, (*a*) a change in the propelling force, the heart-beat, and, most important (*b*), a change in the peripheral resistance.

While elastic tissue is a characteristic feature in the walls of the large arteries, in the arterioles muscular tissue predominates, and gives to these small vessels the important property of *varying their caliber*. With a change in their size, the resistance which they offer to the blood flow also varies; a widespread constriction of the arterioles resulting in a marked rise in arterial pressure, while a great fall accompanies

their general relaxation, for the blood, under these circumstances, flows more readily from the arteries into the capillaries. The highest possible arterial pressure is attained by a general constriction of the arterioles, accompanied by a strong and rapid heart-beat. A very low pressure will result from a general dilatation of the arterioles and a slow, weak heart-beat. If at the same time the walls of the large veins and of the branches of the portal vein relax, the blood will tend to stagnate in these veins, and, since little blood will reach the heart, but little can be pumped into the arteries, in which the pressure will fall to a dangerous extent.

In the adult human the blood-pressure in the terms of a mercury column is about:

— 5— 20	millimeters	in the veins.
0— 50	“	in the auricles.
0—150	“	in left ventricle.
0—110	“	in right ventricle.
110—150	“	in arteries.
25— 50	“	in capillaries.

The arterial blood-pressure rises and falls slightly as a result of **respiration**. The reason for this is that enlargement of the thorax tends not only to cause the inspiration of air, but also to aspirate blood into the intrathoracic veins and heart; while on collapse of the chest during expiration the entrance of blood is less favored, and during forcible expiration is retarded. Consequently, the right heart receives and pumps during inspiration more, and during expiration less, blood into the pulmonary vessels. At the beginning of inspiration there is a slight delay in the reception by the left heart of the surplus blood, for the lungs on inflation accommodate more blood than before, and thus even reduce the amount reaching the left heart. On the other hand, just at the beginning of expiration the supply of blood to the left heart is still further increased, for the excess of blood contained by the inflated lungs, on their collapse, passes to the left heart. The effect, then, on the left heart is that after a slight delay it receives and pumps more blood during inspira-

tion, and thus raises the arterial pressure; while, during expiration, after a momentarily increased supply, it receives and pumps less blood and the arterial pressure falls.

The Pulse.—The blood-pressure and velocity in the arteries varies, of course, with each heart-beat, being greatest during systole, and falling gradually during diastole. In the brachial artery of man the *systolic blood-pressure* is about 35 mm. of mercury higher than the blood-pressure during diastole. This difference is called the *pulse pressure*, and causes the artery to swell slightly with each heart-beat. The impact of this swelling is called the **pulse** and can be felt in all arteries. If an artery is cut it results in the blood flowing in spurts. There is no pulse in the veins.

The pulse is rapidly transmitted throughout the arteries in a wave-like manner, the vessel wall of each succeeding portion expanding as it is reached by the heightened pressure. The slight delay in the transmission of the pulse to the more distant arteries may be readily appreciated by simultaneously feeling the carotid and the radial pulse. Were the arteries rigid tubes, the transmission of the pulse would be instantaneous; and, as it is, the higher the pressure already existing in the arteries, the more rapidly the pulse travels; for when the pressure is high the vessel wall, already tightly stretched, is less capable of further expansion than when the pressure is low. When the pressure is high the pulse will, for the same reason, be small, but it is hard and incompressible as contrasted with the pulse of low pressure, which is large, soft, and easily compressible.

If the **form of the pulse-wave** be recorded (see Fig. 26), it is found to consist in the sudden rapid expansion of the vessel (rise of pressure), followed by a more gradual decrease in size (fall of pressure), the fall being slightly irregular owing to the occurrence of a minor pressure wave. This latter is more prominent when the arterial tension is comparatively low and the heart-beat strong, and is known as the **dicrotic wave**; it originates in the aorta immediately after the closure of the aortic valve, and is transmitted through the arteries in the

wake of the main pulse-wave. It is probably caused by the closure of the semilunar valves.

The Venous Flow.—The blood in the veins flows under very low pressure, for most of the heart-force has been used up in carrying it past the peripheral resistance. Its flow, however, receives material assistance through the contraction of the skeletal and visceral musculature, and through the aspiration of the thorax. When a muscle contracts, it compresses the veins in its neighborhood, and, since they are provided with **valves**, helps to press the blood onward toward the heart. Forcible expiration, of course, retards the passage of blood into the thorax.

The pressure in the distal veins does not fluctuate; is highest at the capillaries and decreases as the heart is approached. At the upper border of the thorax the great veins in the neck show a variation in pressure due to the greater ease of emptying during the inspiratory increase of thoracic negative pressure. On expiration the veins are seen to fill, and on inspiration to empty, giving the appearance of a pulse to this **respiratory variation of pressure**. For about $1\frac{1}{2}$ inches above the thorax the suction effect of the intrathoracic negative pressure is so great as to cause an **intravenous negative pressure** of a slight degree, usually only during inspiration. Some of the veins, particularly the portal system, have been shown to have *vasoconstrictor fibers*.

A true **venous pulse** may occur under two conditions physiologically. If a gland such as the submaxillary is stimulated vigorously to increased activity the freedom of the capillary path through the gland is so great, owing to capillary dilatation, that the arterial pulse is communicated through the capillaries and appears in the veins leaving the gland. The term *venous pulse* though is usually associated with the variations in venous pressure which occur in the jugular vein, synchronous with each heart-beat. There are no valves between these veins and the right auricle, so the intra-auricular pressure variations are transmitted backward by the bloodstream, though modified by the distensibility of the vein

walls. There are two chief waves in the venous pulse. The first, called the *a* wave, is due to the rise in intra-auricular pressure occurring with auricular systole. As the auricle relaxes the pressure falls, but due to the nearness of the carotid artery the thrust of the arterial pulse appears in the record as a wave called *c*, beginning 0.2 second after the beginning of the *a* wave. Intra-auricular pressure continues to fall until the cavity is filled with blood, when it gradually rises again. At the end of ventricular systole the *A-V* valves open and the intra-auricular pressure abruptly falls. The venous pulse accordingly shows a late diastolic rise and an abrupt fall, which is called the *v* wave.

The **coronary circulation** is of considerable importance in relation to the strength of the heart-beat, since it brings oxygen and nourishment to the muscle. Anything interfering with this, as lowered arterial pressure or thickening of the walls of the coronaries, will greatly lessen the heart force. Moreover, since the coronaries are terminal arteries, if they become occluded the area of muscle supplied undergoes necrosis.

An increase in aortic blood-pressure increases the blood supply to the heart muscle, and thus tends to strengthen the beat.

NERVOUS CONTROL OF THE CIRCULATION

The heart is controlled by the central nervous system through two sets of nerves: one set, arising from the cardio-inhibitory center, lessens its activity; the other, carrying impulses from the accelerator or augmentor center, quickens and strengthens the beat. The cardio-inhibitory nerve-fibers reach the heart through the pneumogastric. These are pre-ganglionic fibers and probably exert their influence over the heart muscle not directly, but through the mediation of nerve-cells which are situated in the wall of the organ. These fibers, besides slowing the rate of the heart, cause a weakening in the force of the beat. They affect both the auricular and

the ventricular muscle, but their effect on heart rate is exercised through the medium of the sinus node.

On division of both pneumogastric nerves in the neck the heart beats more rapidly and more strongly, for the tonic controlling influence of the center is thus cut off. If the end of the peripheral portion of one of these divided nerves be stimulated with electric shocks the heart-beat will become slow, or if the current be strong, will stop for a short time. The auricles may in this way be prevented from beating for an hour or more if the stimulation be kept up. The ventricles after a short pause begin to beat of themselves at a slow rate, usually not over 30 per minute, showing that their inherent rhythmicity is too great to be overcome by the vagus.

The **cardio-inhibitory center** is situated in the spinal bulb and is bilateral. It is continually active and its tone may be increased or decreased in a variety of ways; for instance, a rise of arterial pressure increases its activity, the importance of this fact being apparent, for any abnormal rise of pressure will tend to bring about its own fall by lessening the output of the heart through stimulation of this center. The center is also sensitive to the chemical composition of the blood. If the blood becomes unusually venous, the center is stimulated. The center may be stimulated reflexly by various afferent paths, *e. g.*, irritation of the nasal mucosa by vapors, or stimulation of the cutaneous nerves of sensation, or of those from the intestinal tract and lungs which pass through the vagus. These latter fibers cause the slow pulse in peritoneal irritation, or following a strong blow on the abdomen or after forced expiratory movements. This center may be inhibited by afferent impulses, as by those through the glossopharyngeal nerve on swallowing. Inhibition of the center allows the heart to beat more rapidly. The rapid rate after atropin is due to paralysis of the endings of the nerve within the heart.

The **cardio-accelerator center** is probably also situated in the spinal bulb; the nerve-fibers arising from it descend the spinal cord as far as the upper end of the thoracic region, where they probably end, but make physiologic connection in the

gray matter with nerve-cells whose fibers pass out through the upper thoracic ventral nerve-roots; in the dog, through the second and third. They join the sympathetic chain as pre-ganglionic fibers, and probably end in the ganglion stellatum, where a second cell station intervenes, the fibers originating from the ganglion cells passing to the heart muscle. The accelerator center normally sends out tonic impulses, and the heart rate is a balance between these and the impulses from the inhibitory center. Stimulation of the accelerator nerves quickens the rate of the heart-beat after a period of latency, and the effect continues for some time after the stimulus ceases. With the increased rate there is also an increase in the force of the contraction.

This center, too, is sensitive to blood-pressure, being stimulated by a fall. A rise of body (blood) temperature stimulates the center, as does the presence in the blood of the chemical waste products of muscle activity. It can be stimulated reflexly through any afferent nerve, though the vagus effect may predominate. Emotional states readily stimulate it.

The variation of the peripheral resistance is also under the control of the central nervous system. There exists in the spinal bulb a center, known as the **vasoconstrictor center**, which exerts an influence over the muscular walls of the vessels, most evident in the case of the arterioles.

The course of the constrictor nerve-fibers resembles, to a certain extent, that followed by the cardio-accelerator fibers. The nerve-fibers originating in the center pass down the spinal cord, to end in the gray matter at different levels of the thoracic and upper lumbar regions about the nerve-cells, whose axons, usually of small caliber, pass out through the anterior spinal nerve-roots to enter the sympathetic system as preganglionic fibers. The course of the postganglionic fibers to the viscera and head has been described under the Sympathetic Nervous System. As in the case of the cardio-inhibitory center, the activity of this center is continuous and its tone is variable. Like the inhibitory center, it acts as a

regulatory mechanism whereby the blood-pressure is kept fairly constant. If the arterial pressure falls, this center becomes more active and brings about a constriction of the arterioles, thus raising the peripheral resistance, and with it the arterial blood-pressure. It is also stimulated by a venous condition of the blood, the arterial pressure rising to a great height during dyspnea in spite of the simultaneous inhibition of the heart. Its activity is reduced by certain drugs, such as chloroform, ether, alcohol, etc. It may be indirectly stimulated through almost any afferent nerve; for instance, the application of cold to the skin, by stimulating the cutaneous nerves and thus indirectly influencing the constrictor center, brings about a reflex paling of the skin. On the other hand, the application of warmth causes a reflex dilatation of the cutaneous vessels by inhibiting the constrictor center.

The terms *pressor* and *depressor* are used of the effect on blood-pressure produced by stimulating an efferent nerve, and also of the fibers stimulated. Pressure fibers are those which on stimulation produce a reflex vasoconstriction (pressor effect), while depressor fibers produce vasodilatation by inhibiting the vasoconstrictor center (depressor effect).

One afferent nerve which transmits impulses from the aorta to the spinal bulb, and is known as the **depressor nerve**, is of special importance through its relation to this center and consequent influence on the regulation of the blood-pressure. When the arterial pressure rises unduly, the endings of the depressor nerve are stimulated. This results in the passage through the nerve of impulses which, on reaching the bulb, inhibit the constrictor center. The activity of the center being reduced, the arterioles are allowed to dilate, the peripheral resistance is lessened, and the arterial pressure falls. The depressor nerve thus serves as a safeguard against any undue rise of arterial pressure, and affords the heart protection against overwork.

As in the case of the centers which regulate the heart-beat, this center also may be influenced by the emotions; for ex-

ample, blushing is due to its inhibition by nerve impulses descending from the brain.

The control exercised over the vessels by the constrictor center is specialized, for although it maintains a general vascular tone, it need not cause contraction of all the arterioles at the same time; if the vessels of the skin be unusually constricted, those of the viscera are allowed to dilate, and vice versa. This arrangement insures a more even blood-pressure than would otherwise exist.

The blood-supply of the organs of digestion is so large that reflex *splanchnic* vasomotor effects have a profound effect upon the general blood-pressure.

Scattered through the different regions of the spinal cord and bulb are **vasodilator nerve-centers**, whose cells give off axons which, for the most part, follow the same course as the preganglionic vasoconstrictors; no chief vasodilator center has been proved to exist in the bulb. The existence of vasodilator fibers in a mixed nerve-trunk may be demonstrated by special methods of stimulation; there are, however, some nerves which contain vasodilators unmixed with vasoconstrictors. The chorda tympani nerve is one of these, and transmits to the sublingual and submaxillary glands vasodilator fibers which leave the bulb as preganglionic fibers in the seventh cranial nerve. On stimulation of this nerve, the arterioles in the glands dilate and the blood flows through them more rapidly than before. Vasodilatation results in a flushing of the organ, increase in volume, rise in pressure in the veins from the region, or increased venous outflow. By these methods vasodilator fibers have been demonstrated in connection with most of the secretory glands, in the cutaneous vessels, in the abdominal vessels, in the *nervi erigentes*, and elsewhere. Their effect on general blood-pressure is dominated by the vasoconstrictor center, but they are of local importance.

Even at risk of some repetition it seems profitable to review the circulation as a whole, and to note the effect of

variations in the factors by which its efficiency may be influenced.

The **peripheral resistance may be increased**: this leads to a rise of blood-pressure, and this by the depressor nerve mechanism to a reflex vasodilatation which tends to keep the rise of blood-pressure from being excessive. The tonic activity of the vagus is also increased.

A **decrease in the peripheral resistance** results in a fall in blood-pressure. Again the vasomotor mechanism comes to the rescue. The relative anemia of the center causes a vasoconstriction and tends to check the fall in pressure. A higher blood-pressure means **increased blood-flow in the coronary vessels**, and this leads to a better nourishment of the heart muscle. A stronger contraction is developed; the muscle tone is increased.

The **heart rate** is never affected without the vasomotor mechanism being involved in the same reflex. Vagus and vasoconstrictor tone are affected similarly, so that the heart is slowed and the blood-pressure raised, or vice versâ. It is found experimentally that varying the rate alone within normal limits does not vary the heart's output per minute.

The **output per minute** of the heart is the factor which maintains the circulation, and if the muscle is intact is independent of heart rate and of arterial pressure. It varies entirely with the amount of blood coming to the heart through the veins. This **venous inflow** can, of course, be decreased by high peripheral resistance, by low arterial pressure without vasodilatation, by great dilatation of the walls of the large blood-vessels, or by decreased blood volume as in hemorrhage.

The amount of **energy which the heart muscle can develop** is greater as the cavity increases in size up to a certain optimum, beyond which further increase in size puts the muscle at increasing mechanical disadvantage. The **cardiac tone**, by which is meant the size of the heart, both during systole and diastole, is governed by the amount of blood which it must put out with each beat in order to keep pace

with the venous inflow and by the functional integrity of the muscle. The **output per beat** is decreased with increasing rate, and vice versa, so that with constant venous inflow the heart *must* be larger (*decreased tone*) *with slow rates* than with more rapid rates, so that the increased size may allow it to develop the greater energy necessary for the greater output per beat. If the **integrity of the muscle** is impaired, it cannot eject all of the blood coming to it from the veins. Both at the end of systole and of diastole the volume will be larger—the tone is decreased—and the increased size of the heart enables the muscle to develop increased energy enough to maintain the same output as before. Cardiac failure ensues when this dilatation reaches the point where further increase in size is not of further mechanical advantage.

Besides its effect on heart rate, the **vagus** also has an effect upon the development of energy by the muscle. It causes a slower development of the contraction, less force is exerted, and the contractile stress passes off more slowly. The **accelerator mechanism** also affects the contraction, and in an exactly opposite manner to the vagus.

Accompanying a slow heart rate then, we find a larger heart, higher venous pressure, a greater pulse pressure, but blood-pressure and blood-flow remaining constant. With rapid rate these conditions are reversed.

QUESTIONS FOR CHAPTER VII

What determines the moment at which any cardiac valve opens and closes?

Why are the auriculoventricular and semilunar valves never open at the same time?

Does blood enter or leave the ventricle in the interval between the first and second heart-sounds?

Does blood enter or leave the ventricle in the interval between the second and first sounds?

If the auriculoventricular valves be insufficient, during what period of the heart cycle will blood escape from the ventricle into the auricle?

If the aortic valve be insufficient, during what period of the cycle will blood flow back from the aorta into the ventricle?

Of what accompanying event should we make use in distinguishing the first from the second heart-sound?

If while the force which propels liquid through a tube remains constant the resistance be varied, how is the expenditure of the propelling force modified?

Why is the pressure in the aorta higher than that in the small arteries?

Which travels most rapidly, the pulse or the blood-stream?

When the pulse is large, what is the condition of the arterioles?

When the heart is beating strongly, how can you determine the extent of vascular tone?

What sort of pulse accompanies dyspnea?

Why should the diastole of the pulse be exaggerated when the peripheral resistance is low?

What different circumstances tend to the production of a capillary pulse?

How does it happen that not only the auricle but the ventricle also beats more slowly during increased activity of the inhibitory center?

What is the result of inhibiting the cardio-inhibitory center?

Why should division of both pneumogastric nerves lower the pressure in the large veins?

In what respect would the regulation of the blood-pressure be modified by destruction of the cardio-inhibitory center?

Why should compression of the aorta cause the heart to beat more slowly?

Through what two channels may one organ influence another?

How is the blood-flow through the small vessels affected by loss of arterial elasticity?

What importance do you attach to the position of a patient during chloroform or ether anesthesia?

Compare the effects on blood pressure of the division of the spinal cord in the cervical and in the lumbar regions.

How many neurons are concerned in the control exercised by the constrictor center over a single arteriole?

How can it be determined whether the control exercised by a center is continuous?

How does bleeding modify vascular tone?

How does indirect differ from direct stimulation of a center?

What conditions of the circulatory system may lead to fainting?

Of what importance is the intracapillary blood-pressure?

If all the nerves of a limb have been divided, would it be possible by causing the muscles of this limb to perform work to influence the heart-beat?

How does severe hemorrhage cause dilution of the blood?

How does a rise of arterial pressure tend to concentrate the blood?

How does the concentration of the blood tend toward a rise of blood-pressure?

What nervous mechanism opposes these two tendencies?

In what particulars is the existence of the vasoconstrictor center a source of economy to the body?

What different vascular conditions may lead to a paling of the face?

What class of vessels is the seat of every important alteration in the composition of the blood?

In what organ is lymph most rapidly formed?

In the absence of the vasoconstrictor center, how could the blood-supply of a given organ be modified according to its needs?

In what respect would the regulation of the blood-pressure be interfered with by division of both depressor nerves?

Would the division of the cervical sympathetic nerve have any effect on the color of the face?

Would you class the vasodilators as vasomotor nerves?

Is constant standing or walking the more productive of varicose veins?

How can we afford the greatest voluntary assistance to the entrance of venous blood into the heart?

Why does putting a cold object, such as a key, down the back tend to stop epistaxis?

How are the lower limbs affected by compression of the iliac veins?

How would you expect the size of the heart to vary during dyspnea?

What effect on intrathoracic pressure has the systole of the ventricles?

If the heart be emptied of blood and be caused to beat, which of the heart-sounds will be heard?

How do you know that the slow rate of blood-flow through the capillary district is due to the width of bed and not to resistance?

Explain the occurrence of a venous pulse.

Trace the course of the blood in the adult, and in the fetus. Where is the highest pressure to be found and during what phase of the cardiac cycle?

Of what advantage are a slow rate and low pressure in the capillaries?

Describe the course which the contraction takes in passing over the cardiac muscle.

How can we determine whether the heart produces electricity when it contracts?

What is the difference between systolic, diastolic, and pulse pressure?

What is the total effect upon the circulation of a pressor nerve impulse?

When there is a large hemorrhage, what is the effect upon the circulation?

Why does a heart having weakened muscle change its size, and what is the change?

Does the vagus or accelerator mechanism affect anything except the heart rate?

CHAPTER VIII

DIGESTION AND ABSORPTION

DIGESTION consists in the physical and chemical alteration of food, with the object of obtaining products which will be more easily absorbed into the blood-stream or more easily utilized by the body than the food-stuffs as they are originally taken. In order that it may be absorbed food must be made soluble.

Mechanical subdivision of the food is necessary or helpful in that it breaks up large masses and allows a greater surface for the digestive juices to act upon; it also facilitates solution of soluble substances. In the case of the insoluble food-stuffs a change in composition is necessary so that they shall become soluble. This change is affected by the enzymes and bacteria of the digestive tract.

MOVEMENTS OF DIGESTION

Digestive Juices.—The first process to which food is subjected is **mastication**. This is the function of the jaws and teeth, while the tongue, cheeks, and lips serve to keep the food in place so the teeth may act upon it.

The food is thus not only ground up, but is mixed with the saliva and collected together in a mass or **bolus** which is swallowed. Only the first of the movements which play a part in deglutition are voluntary. If the mouth be empty of anything that could be swallowed, including saliva, it is impossible to voluntarily provoke all the swallowing movements. They are for the most part purely reflex, and are excited through the afferent nerves of the soft palate, of the back of the tongue, and of the fauces, which are stimulated by the contact of any substance with the mucous membrane

covering these parts. The first part of the action, which may be accomplished voluntarily, consists in the approximation of the tip of the tongue to the hard palate, followed by a raising of the floor of the mouth and tongue by the contraction of the mylohyoid muscles. The levatores palati also contract and raise the soft palate against the posterior pillars of the fauces and the posterior wall of the pharynx, thus shutting off the nasal cavity. The food is forced back by the tongue, etc., through the fauces into the pharynx. Its entrance into the larynx is prevented both by the contraction of the crico-arytenoid muscles, which pull the posterior border of the opening of the larynx forward, and by the thyrohyoid muscles, which raise the larynx so that the epiglottis is closed back over it. At the same time the glottis is closed, and the respiratory center inhibited through the glossopharyngeal nerve.

The downward passage of solid food is furthered by the contraction of the constrictors of the pharynx and the esophageal muscles, this contraction progressing in a wave-like manner and taking six seconds to pass from pharynx to cardia. These muscles also contract on the deglutition of liquid, though their assistance seems to be unnecessary for liquids reach the cardia in 0.1 second, being apparently shot through the esophagus by the force of the initial act of swallowing. If successive mouthfuls be swallowed at intervals of less than 6 seconds, the esophageal muscles are inhibited and remain lax, so that the first bolus waits for the arrival of the second before passing into the stomach. The cardia relaxes when the bolus reaches it and allows the food to pass into the stomach.

The center (or centers) controlling deglutition is situated in the spinal bulb; the afferent nerves concerned in the reflex are the fifth and ninth cranial nerves and the superior laryngeal branch of the tenth; the artificial stimulation of this latter nerve may cause swallowing movements when the pharynx is empty.

The **stomach** may be divided on physiologic grounds into

three parts. The first, or **fundus**, is the large rounded portion which lies to the left of the cardia. It is not plainly demarcated from the **body** or **prepyloric region**, but this latter is marked off from the **pyloric antrum** by a slight constriction known as the transverse band. The function of the stomach consists in receiving the food and retaining it for a period of four or five hours, so that it may be thoroughly softened and mixed with the acid gastric juice.

A few minutes after food enters the stomach small contractions of the circular fibers start in the middle region and run toward the pylorus. In man these contractions start about once every twenty seconds, and as digestion proceeds they increase in frequency and, more especially, in extent of contraction. The fundus region and first part of the prepyloric region do not show these circular contractions, but maintain a tonic contraction varying in intensity, which, the cardia being closed, tends to always press more food into the active part of the stomach.

The progressing waves or rings of contraction tend to press the contents of the pyloric part of the stomach against the pyloric sphincter. At certain intervals this sphincter relaxes, so that the stomach contents are pressed into the duodenum. The relaxation of the sphincter is a reflex mechanism depending upon the *acidity* and *consistency* of the material pressed against it. Liquid food passes readily through the pylorus, so that liquids taken with a meal are mostly passed around the more solid part and out of the pylorus. Hydrochloric acid in the stomach favors relaxation of the pylorus, but in the duodenum it causes a contraction of the sphincter.

As, then, the food is mixed with the gastric juice in the intermediate and pyloric portions of the stomach so that it has the proper chemical composition and has been reduced to a thin liquid, it is passed along into the duodenum. This thin gastric contents is called "chyme." The various food-stuffs, if fed separately, are retained for different periods in the stomach. Carbohydrates are retained but a short time,

proteins longer, and fats for a considerable time. Mixtures are retained depending upon the relative amounts of the various ingredients.

The gastric and pyloric mechanism is essentially automatic, being the result of inherent impulses which are most likely mediated through the intrinsic nerve ganglia (plexuses of Meissner and Auerbach). They are probably of reflex origin from the gastric mucosa, but possibly are due to the inherent automaticity of the plain muscle.

The stomach receives *extrinsic nerves* from the vagus, stimulation of which produces an increased motility, and from the sympathetic gangliated cord through the splanchnic nerves, stimulation of which produces a dilatation of the stomach and relaxation of the pylorus. Through these nerves the gastric motility may be influenced by reflexes passing through the central nervous system, and by the emotions.

In the **duodenum** the chyme encounters the bile and the pancreatic juice and the succus entericus secreted by the cells of the intestinal mucous membrane. Its acidity is promptly neutralized, and it is subjected to further propulsion, which passes it along the small intestine to the cecum, and during this passage digestion continues and absorption takes place. The *movements of the small intestine* are of two main types, *rhythmic and peristaltic*. The rhythmic movements consist in the contraction of adjacent bands of circular fibers upon a mass of the intestinal contents so as to divide it again and again into different parts. The peristaltic movements consist in a circular contraction preceded by a region of dilatation, which, beginning at any point of the intestine, progresses toward the ileocecal valve, the muscle relaxing again when the contraction passes on to the next segment. The peristaltic wave drives the food along for a distance and leaves it, whereupon it is subjected to the rhythmic movements until peristalsis takes it up again. From three to five hours are necessary for the passage of food from the stomach to the cecum. The part played by the

longitudinal fibers is not clear, but they tend to move the intestine about, giving a sort of writhing motion which may facilitate the movement of the food. Antiperistalsis is a term meaning the same type of contraction, but running toward the stomach. It does not occur normally.

The regulation of these movements is not clearly understood, but it is possible that the rhythmic contractions are of muscular origin due to the distention by contained food, while the peristaltic movement is a reflex effect from the mucous membrane conducted through the intrinsic nerve plexuses. As in the stomach there are extrinsic nerve-fibers through the vagus, mainly motor in effect, and through the splanchnics from the sympathetic chain, which have an inhibitory action. These fibers emerge in the sixth dorsal to the first lumbar spinal nerves, and serve to place the intestines under reflex control of the central nervous system. It is probably through the spinal cord centers and splanchnics that the intestines are inhibited when there is inflammatory disease of the peritoneum. Violent movements are produced by shutting off the blood-supply. CO_2 , CH_4 , and H_2S gases within the bowels act as stimuli to peristalsis, as does a bolus of food and the organic acids, such as acetic or formic, which may be formed normally in the intestine by bacterial fermentation of carbohydrate.

The **large intestine** shows two general types of movement. In the ascending and proximal part of the transverse colon the most frequent movement is antiperistalsis, tending to force the food back against the ileocecal valve which prevents its reflux into the ileum. These waves occur in groups, with intervening periods of rest. The progress of the food toward the rectum is thus delayed so as to allow time for further digestion, and especially for absorption. As the colon becomes filled, the more solid parts of the food residue (feces) are taken up by rather strong but slow peristaltic waves in the transverse colon and carried to the sigmoid and rectum. This mechanism also is inherent, but is regulated by paths from the second to fifth lumbar nerves, whose

postganglionic fibers start in the inferior mesenteric ganglia and form part of the hypogastric plexus. These fibers are inhibitory, but fibers leaving the cord in the second to fourth sacral nerves and forming part of the nervi erigentes and of the hypogastric plexus have a motor or augmentor effect.

Defecation seems dependent on afferent impulses due to a distention of the rectum. The internal sphincter, being smooth muscle and not under control of the will, is thrown into tonic contractions by these impulses. The external sphincter, of voluntary striate muscle, is normally in tonic contraction. The act of defecation is probably at bottom an intrinsic involuntary reflex, with a governing center in the lumbar cord. Though involuntary, this reflex can be to a certain extent inhibited by the will, and we can also voluntarily increase the tone of the external sphincter. The act is accomplished by peristalsis of the sigmoid and rectum, aided by an increased tension of the abdominal muscles and relaxation of the two sphincters. The feces are thus forced through the anus. The rectum and internal sphincter receive motor fibers via the nervus erigens, and inhibitory fibers via the hypogastric nerve, both from the hypogastric plexus.

Vomiting is a very complicated reflex, usually preceded by a sensation of nausea. Next follow the movements of retching, strong inspirations with narrowed glottis, and during one of these movements there is a strong contraction of the abdominal muscles which forces the stomach contents out through the relaxed cardia and esophagus. The stomach is not believed to take an active part, except that its pyloric end is strongly contracted to prevent the contents passing into the duodenum. Vomiting is produced by afferent impulses from the mucous membrane of the alimentary tract (glossopharyngeal and vagus nerves) or from any of the abdominal viscera (vagus). It may also result from psychic states, as vertigo, or from pressure upon the brain. This latter fact has led to the suggestion of a vomiting center in the medulla, and surely such a complicated act must be under control of some coördinating center.

THE DIGESTIVE FLUIDS AND ENZYMES

Saliva is the first of the digestive secretions to be encountered by the food. It is a colorless, viscid, faintly alkaline liquid, containing mucin, inorganic salts, and two enzymes, ptyalin and maltase. It is mixed with the food by the teeth and tongue, and serves to dissolve some of the food elements and to soften others. Saliva is produced by the parotid, submaxillary, and sublingual glands. These glands receive two sets of secretory nerves, cranial and sympathetic. The cranial nerve-fibers (preganglionic), which innervate the parotid, leave the bulb in the ninth cranial nerve and probably end in the otic ganglion in contact relations with nerve-cells whose axons (postganglionic) reach the parotid through the auriculotemporal branch of the inferior division of the fifth nerve. The cranial fibers which control the submaxillary and sublingual glands emerge from the bulb in the facial nerve, and, by way of the chorda tympani, reach the submaxillary and sublingual ganglia. In these ganglia they end, and make physiologic connection with cells whose postganglionic fibers are distributed to the gland-cells. Postganglionic sympathetic nerve-fibers from the superior cervical sympathetic ganglion are supplied to each of these glands. The cranial secretory fibers are accompanied by vasodilator fibers; the sympathetic, by vasoconstrictors.

Artificial stimulation of the **chorda tympani** produces a result which differs widely from the effect of stimulating the **cervical sympathetic**. In the former case the submaxillary gland secretes abundant watery saliva, in the latter case the secretion is thick and scanty. Stimulation of the chorda tympani, of course, increases the blood-supply of the gland and thus renders a copious secretion possible, but the variation of the blood-supply probably does not account altogether for the difference in the two results.

That the cause of the salivary secretion is not wholly the filtration effected through the gland substance by the arterial blood-pressure is shown by the fact that the pressure in the

salivary duct, if it is occluded, can readily be raised above the carotid blood-pressure by stimulation of the chorda tympani nerve, and additional proof is that for a considerable time after the gland is removed from the body or separated from its vascular connections stimulation of the chorda tympani nerve causes an active secretion of saliva.

The normal secretion of saliva is a **reflex** event. It is readily initiated by stimulation of the terminations of the afferent nerves of the oral mucous membrane by food or other substances placed in the mouth, weak acids forming a particularly effective stimulus. Reflex secretion of saliva is brought about only through the cranial nerve-fibers. The salivary centers are not under the control of the will, but by thinking of food we may cause the dispatch of involuntary nerve impulses from the brain to the salivary centers, and thus indirectly bring about a flow of saliva. These centers may be not only excited by psychic states, as by the sight or smell of food, but they may also be inhibited, as by fear or nervous worry.

Ptyalin is the chief enzyme of saliva. It is also called salivary diastase, and its action is to convert starch into maltose and dextrin, which it does by hydrolysis. Only starch, the granules of which have been ruptured by boiling or by the teeth, can be attacked by ptyalin. There is a small amount of **maltase** present in saliva which may act on the maltose and hydrolyze it still further to dextrose. These ferments act only in an alkaline medium and, therefore, only in the mouth and in the portion of the fundus of the stomach to which the acid gastric juice has not yet penetrated.

In the stomach the **gastric juice** is secreted by the tubular glands of the mucosa. It is a thin liquid, containing HCl to the extent of 0.3 to 0.5 per cent., some protein, mucin, and inorganic salts, and two, possibly three, enzymes, pepsin, rennin, and lipase. The acid is secreted chiefly in the middle part of the stomach, where the peculiar "cover cells" are much more numerous in the glands. Gastric juice initiates

the digestion of protein and is produced in response to efferent impulses passing in the vagus. These impulses arise as reflexes from the taste and smell sensations which go with eating (*psychic secretion*). After the food reaches the stomach the gastric secretion continues in response to a hormone (*gastric secretin*), which results from the action of certain food products, called *secretagogues*, upon the mucosa of the pyloric region. The quantity and quality of the secretion varies with the sort of food—specific excitatory action of the secretagogues—and the quantity of secretion with the amount of food. Secretion may be inhibited by psychic stimuli.

Pepsin is a proteolytic enzyme which acts only in an acid medium. It changes the proteins of the food to simpler forms by a process of hydrolysis. The end-products are called peptones, which though still protein in structure are much less complex and are very soluble. The acidity of the secretion assists in the early stages of the hydrolysis. Peptic digestion is of value not only from the protein hydrolysis it causes, but also from the fact that proteins which have been subjected to it are more easily and thoroughly digested by the intestinal enzymes.

Rennin (rennet) is an enzyme which has the peculiar property of causing milk to set in a jelly-like coagulum. The casein of milk is converted by the rennin to a substance (paracasein) which unites with the calcium salts present in milk to form an insoluble compound, the curd or clot. Without the calcium this will not take place. It is not a process of digestion, but may aid the digestion of the casein. The gastric **lipase** is relatively unimportant, though it does hydrolyze some of the fat of the food.

In the intestine the food encounters three separate secretions, that of the pancreas, that of the liver, and that of the intestinal mucosa, which, acting in combination, perform the major part of digestion.

The **pancreatic juice** is a thin, watery, alkaline liquid which is secreted by the cells of the pancreas. It contains three

enzymes—or their zymogens—trypsin, amylopsin, and steapsin. The pancreatic secretion is controlled by secretory fibers which run in the vagus, but is produced chiefly in response to chemical stimulation of the gland cells by a *hormone*, called *pancreatic secretin*. This is formed by the action of the acid of the gastric juice upon a substance, *prosecretin*, which is secreted by the duodenal mucosa. The pancreatic juice, like the gastric, varies in quantity and quality with the type of food ingested.

Trypsin is not secreted as such, but as a zymogen, which is converted to trypsin by a kinase (*enterokinase*) produced by the intestinal mucosa. Trypsin is a proteolytic enzyme which acts much as pepsin, but more powerfully, and which acts in an alkaline medium. It completes the hydrolysis begun by pepsin, and, as has been stated, acts better on protein which has previously been subjected to gastric digestion. It hydrolyzes beyond the peptone stage, producing the amino-acids, substances which are very soluble, crystalline, and no longer protein in nature.

Amylopsin is a diastatic ferment with an action almost identical with that of ptyalin, having maltose and dextrin as end-products. **Steapsin** is a lipolytic enzyme which hydrolyzes the neutral fats, producing fatty acids and glycerin. The fatty acids form soaps with the intestinal bases, and these soaps emulsify the remaining neutral fat, so that they are more readily acted on by the ferment.

Mixtures of pancreatic lipase (steapsin) with bile are much more effectual than the pancreatic juice alone. **Bile** is a mucilaginous, golden-yellow, alkaline fluid containing about 2.5 per cent. solids, of which the chief are bile salts, pigments, and inorganic salts; fatty acids, lecithin, and cholesterol are present in lesser amounts. Bile constitutes the external secretion of the hepatic cells passing into the hepatic ducts. Though it is formed continuously, it is not in man discharged continuously into the duodenum. The opening at the papilla of Vater is usually closed by the tonic contraction of its smooth muscle-fibers, so that the bile passes back

through the cystic duct to be stored in the readily distensible *gall-bladder*. The presence of chyme in the duodenum acts reflexly through the splanchnics to relax this sphincter and to cause a contraction of the gall-bladder. Thus, bile is discharged only during the period of digestion.

If the bile-ducts are obstructed, bile will continue to be secreted and is absorbed into the blood-stream by way of the lymphatics of the liver. Bile-pigments in the blood and tissues produce a condition called *jaundice*. The actual secretion of bile seems not to be under nervous control, though factors increasing the blood-flow through the liver also increase the bile, and vice versâ. Certain substances in the blood-stream increase the flow of bile. They are called *cholagogues*, and include bile salts, bile-pigments, hemoglobin dissolved in the plasma by any hemolytic agent, pancreatic secretin, etc.

Bile is important as a digestive secretion in that (1) it aids in the neutralization of the acid chyme; (2) the bile salts facilitate the action of the pancreatic lipase; (3) it aids in the absorption of fatty acids by making them soluble; (4) in some way it decreases the intestinal putrefaction, though not itself an antiseptic.

Bile is also important as an excretion, under which head the sources of its constituents will be considered.

The secretion of the intestinal mucosa, **succus entericus**, has only a feeble digestive action, except upon the starches. Extracts from the mucous membrane, however, or juice squeezed from it, shows, besides the *prosecretin* and *enterokinase* already mentioned, *five enzymes*: **Erepsin**, a proteolytic enzyme, which acts to convert peptones to the amino-acids, **maltase**, **invertase**, and **lactase**, the so-called inverting enzymes, which convert the disaccharids, maltose, sucrose, and lactose, to the monosaccharids, dextrose, levulose, and galactose, **Nuclease**, an enzyme which further splits the nucleic acid which has been separated from the nuclein molecule by the pepsin-trypsin digestion.

When the food reaches the cecum it is quite fluid and diges-

tion is practically complete. It remains in the ascending colon for some time though, and the intestinal ferments continue their action here. In the small intestine only those bacteria capable of fermenting carbohydrates are active, but here the putrefactive bacteria are predominant, breaking down any protein present to such products as indol, skatol, phenol, CO_2 , H_2S , etc. Many of these pass out in the feces, but some are absorbed and excreted in the urine. The necessity or harmfulness of this putrefaction is still debated.

DIGESTION AND ABSORPTION OF FOOD MATERIALS

Carbohydrates are acted on by ptyalin in the mouth and in the fundus of the stomach before being acidified. Only the soluble polysaccharids are affected, *i. e.*, not cellulose, and the process does not go beyond the stage of maltose and achröodextrin. The pancreatic amylopsin takes up and completes this function in the intestine with the same end-products, which though they can be absorbed cannot be utilized by the body. They are never found in the blood except when taken in great excess. The inverting enzymes of the intestinal wall change the disaccharids to monosaccharids, the normal state for carbohydrate absorption. The absorption takes place mostly in the small intestine, but is completed in the ascending colon. Fermenting bacteria may reduce a small amount. About 3 per cent. of ingested carbohydrate can be recovered from the stools.

Fats are not digested until they reach the intestine, by which time they have been liquefied by warming and somewhat emulsified by the motion and acid of the stomach. Steapsin hydrolyzes this emulsion and the fatty acids resulting from soaps, which still further emulsify. Glycerin and fatty acids are the end-products. The fatty acids are made soluble by the presence of bile salts, and are absorbed along with the glycerin by the cells of the intestinal epithelium. These cells produce within themselves from the absorbed fragments a new fat, of the type predominant in the organism to which they belong. This fat is extruded into the lymph-

spaces and carried in the form of a very fine emulsion through the lacteals to the thoracic duct, which empties it into the blood-stream. Some of the fat enters the blood from the lymph-spaces and is carried to the liver by the portal vein. About 5 per cent. of the fat taken as food may be recovered from the stools.

Protein digestion is started by the acid and pepsin of the stomach, and is completed by the trypsin and erepsin of the intestine. Amino-acids are the end-products which are absorbed, but their further history is still debated. In all probability they are carried in the portal blood to the liver and thence distributed all over the body, though it has been contended that they are resynthesized in the intestinal mucosa into the specific serum-albumin of the organism. About 8 per cent. of the ingested protein is found in the stools.

Water and inorganic salts are not absorbed in the stomach, but are absorbed throughout the intestine. The final absorption of water takes place in the large intestine, and the residues of digestion constitute the **feces**. These contain the indigestible ligamentous tissue of meat, cellulose, unruptured starch grains, a small amount of meat fiber, some soluble carbohydrate and some neutral fats, fatty acids, and soaps. There is also unabsorbed detritus from the intestinal epithelium, products of bacterial putrefaction, a pigment **sterco-bilin**, derived from the bile-pigments by reduction, inorganic salts, and great quantities of bacteria. There is also a variable amount of gases due to fermentation and putrefaction, as CH_4 , CO_2 , H_2 , N_2 , and H_2S . The fecal odor is chiefly due to H_2S and skatol.

QUESTIONS FOR CHAPTER VIII

What foods actually require digestion before they can be absorbed?

Does protein undergo any preparation for absorption in the mouth?

If raw starch and saliva be mixed, will the digestion of the former be assisted by boiling the mixture?

If starch paste be acidified with HCl , the addition of what substance will enable saliva to digest the starch?

If starch and saliva be mixed, and a drop of the mixture be tested at intervals with iodine solution, why does the color reaction vary?

What step in digestion which is of more importance than the salivary digestion of starch is carried on in the mouth?

Why is it well to wash the teeth after each meal?

What secretion possesses the widest range of digestive power?

Can you readily arrange the digestive secretions in the order of their relative importance?

How is digestion affected by removal of the stomach?

In what respect is digestion most interfered with by removal of the pancreas?

Which of the following substances are of equal value as food, whether they be injected directly into the blood-stream or introduced into the alimentary canal: dextrose, cane-sugar, soluble starch, lactose, egg-albumen, peptones, raw serum-albumin, cooked serum-albumin, levulose?

Supposing that pyloric and duodenal fistulae have been established, so that there is no communication between the stomach and intestines, the animal may be fed through the mouth, or by introducing food and water directly into the duodenum. Which method of feeding will prove the more satisfactory?

What effect on digestion has the existence of a biliary fistula?

How does fat reach the blood-stream?

How is digestion modified by the absence of hydrochloric acid from the gastric juice?

What constituents of food require no digestion?

What different factors play a part in determining the reaction of the intestinal contents?

Under what circumstances does glycerin appear in the intestines?

Where and how is bread and butter digested?

Why is it impossible to swallow six times in rapid succession without plunging something in the mouth?

Have the emotions any influence over digestion, and is the effect of all emotions the same?

Why should the addition of horn shavings, which are indigestible, enable a rabbit to live on a milk diet?

How is it that protein food does not result in peptone-poisoning?

If soluble starch is absorbed from the intestine, why does it not appear in the blood?

What evidence of constipation may be shown by the urine?

What instances of synthesis in the body can you mention?

Name the three portions of the stomach, and describe the function fulfilled by each.

In what way do the gastric and the intestinal movements differ?

Why does some food pass the pylorus more readily than other food?

From whence is the stimulus which causes the movements of the intestine?

What is the characteristic feature of the movements of the large intestine?

Name the enzymes found in the intestine; what is the action of each?

What is the mechanism concerned in the flow of saliva?

What causes the flow of gastric juice? Of pancreatic juice?

Is bile a digestive secretion?

Has the large intestine an important function in digestion?

What is found in the feces?

CHAPTER IX

METABOLISM, NUTRITION, AND ANIMAL HEAT

THE food, after digestion and absorption, reaches the lymph-spaces of the gastric and intestinal mucous membranes. The proteins and carbohydrates pass, for the most part, from the lymph into the blood-capillaries, and are carried through the portal vessels to the liver; the fat, for the most part, reaches the subclavian vein through the lymphatic vessels. Let us consider the further fate of these substances in the body.

As we have seen, the **carbohydrates** reach the blood chiefly in the form of dextrose, though there is also some lactose and galactose. If during digestion samples of blood be taken from the portal and hepatic veins and compared, it will be found that the hepatic blood contains the smaller percentage of sugar. Evidently, then, sugar disappears from the blood as it passes through the liver. If the liver of a well-fed animal be examined with the microscope, the liver-cells will be seen to contain an opalescent substance, which lies in that portion of the cell adjacent to the blood-capillary. On treatment with iodine this substance gives a port-wine color reaction, resembling that given with iodine by erythrodextrin. It is the carbohydrate *glycogen*. Like starch, glycogen is non-dialyzable; unlike starch, it is readily soluble.

Not all the carbohydrate which reaches the liver is converted into glycogen; a large proportion passes through the liver unchanged and is distributed through the arteries to the system in general. It is rapidly taken up from the lymph by the muscles, a certain amount being converted

into and stored as glycogen by them. Taken collectively, the muscles may contain as much glycogen as is found in the liver, but in muscle the percentage is smaller—1 to 4 per cent. in liver *vs.* 0.5 per cent. in muscle.

The muscles store the glycogen which they need for their own oxidations, but the liver acts as a storage point for the whole body. It retains glycogen as long as the dextrose in the blood is at its normal concentration (0.1–0.2 per cent.), but if this percentage is decreased by the tissues removing dextrose for their uses, the liver glycogen is converted to dextrose, in this way maintaining the normal concentration of this substance in the blood. This function of the liver is most important and is brought about by an enzyme, *liver diastase*. This function is, however, under nervous control, for puncture of a certain area in the medulla, between the nuclei of the sixth and tenth cranial nerves, causes the liver to discharge all of its glycogen into the blood as glucose. A similar result may be obtained by stimulating the afferent fibers of the vagus, and of certain other nerves. If the splanchnic nerves are cut this effect cannot be obtained, so that this seems to be the course of the efferent fibers.

The ultimate oxidation of carbohydrates takes place in the tissues, and the muscles being the most active tissues are most prominent in carbohydrate oxidation. Carbohydrates are the most readily oxidizable of the food materials, and are the chief source of energy to the body tissues. The monosaccharids, glucose especially, are oxidized to form **water** and **carbon dioxide**, and the internal secretion of the pancreas, a **hormone**, is necessary for this process. *Lactic acid* is a prominent feature of the intermediary chemical process, and it is probable that formic, glycuronic, and oxalic acids are also formed. The stored glycogen is converted to glucose before oxidation. This oxidation is an exothermic process and plays a most important part in the production of the heat necessary to maintain body temperature (*q. v.*).

If the body is supplied with carbohydrate in excess of its

ability to store up glycogen, some is converted into and stored as fat. If carbohydrate is deficient, the glycogen store is first exhausted, and then fat and protein are broken down in excessive amounts to produce heat and energy, the protein yielding any contained carbohydrate radicals to maintain the glucose percentage of the blood. When carbohydrate is supplied in normal amounts it seems to act in a sparing or protective manner upon fat and protein, *i. e.*, it is oxidized by preference, so that the other materials are called upon to a lesser extent. This is especially true during violent exercise, when the call for oxidizable material is greatest.

The pouring out of dextrose into the blood, which follows upon puncture of the medullary area mentioned, is so rapid that the dextrose cannot be oxidized or excreted fast enough to keep pace with it. The percentage of dextrose in the blood is increased above normal, a condition known as **Hyperglycemia**. Hyperglycemia may also result from a large ingestion of mono- or disaccharids. In this case the liver and muscles are unable to quickly enough convert to glycogen or to oxidize the large amount of sugar which is absorbed. Polysaccharids (starch) cannot produce this *alimentary hyperglycemia*, because they are so slowly converted to the absorbable monosaccharids that the tissues can handle the latter as they receive them. Inability on the part of the tissues to oxidize glucose also results in hyperglycemia, but the mechanism of its production is not known. This is the situation in *diabetes mellitus*, called pancreatic diabetes because the pancreatic hormone necessary for the oxidation of the glucose is supposed to be deficient. At times levulose can be oxidized by a diabetic patient when glucose cannot.

Fat reaches the blood-stream mostly by way of the thoracic duct, but some is carried from the intestines to the liver by the portal blood. Fat is removed from the blood by the tissues which can use it, and is either *oxidized* to form energy, or if the present energy needs are satisfied, it is *stored up* as a fuel reserve in the adipose tissue of the body.

The oxidation of fat results in the production of *carbon dioxide* and *water*, and the setting free of much *energy*, more than twice as much weight for weight as carbohydrate or protein. The steps of the oxidation are not known, but there is a lipolytic enzyme in many of the body tissues, so that the first step is supposed to be a splitting to glycerin and fatty acid.

When, as in starvation, fevers, and diabetes mellitus, there is a very large call upon the fat reserve of the body to supply energy, we find certain bodies in the blood and urine, β -oxybutyric acid, diacetic acid, and acetone, called the **acetone bodies**. They are supposed to be the result of incomplete oxidation of the fatty acids. The liver plays some part in fat-metabolism, though exactly what part is unknown.

The body fat results partly from the fat of the food and partly from carbohydrate and the oxyacid radicals of protein. Its *functions* are to provide a reserve store of energy, to provide heat by its oxidation, to be synthetized into more complex bodies as lecithin, and to protect from oxidation the body protein just as does carbohydrates, though less readily.

Protein reaches the blood-stream in the form of its constituent parts, the amino-acids. The tissues which need these take them up and construct from them new protein tissue for purposes of growth and repair. The amino-acids not so used are of no value to the body except as a source of energy, and are accordingly oxidized. The nitrogen portion is first split off as *urea* or *ammonium salts*, and these are discharged into the blood and excreted. This takes place mostly in the liver, but also in all the tissues which can use the amin bodies, especially in muscle. The liver converts much of the ammonium salts to urea, so that 80 to 85 per cent. of the nitrogen excreted is in this form, and only 5 to 6 per cent. is excreted as ammonia salts.

The other part of the amino-acid molecule, an organic acid group, is either oxidized to CO_2 and water, or converted to glycogen or fat and stored in this form. This

explains why the urea excretion varies with the amount of protein in the food.

There are other more complex nitrogenous bodies which are excreted, *creatinin* and the *purin bases*, which do not vary with variations in the protein intake unless food containing them is eaten. These are considered to arise from the breaking down of the living tissues, and to represent the wear and tear of the living machinery. The tissue protein is estimated to break down at about 1 per cent. per diem. The nucleic acid radical of the nucleoprotein of the tissues is split by nuclease to form the amino-purins, and these by further enzyme action (adenase, guanase, oxydase) are converted to xanthin, hypoxanthin, and uric acid. In man about half of the uric acid thus formed is converted by urease to urea before excretion, while the protein portion of the nucleoprotein molecule also furnished urea. The tissue nucleoprotein taking chief part in the production of uric acid is that of the muscles, since they are the tissues which are most active. For the same reason most, if not all, of the creatinin comes from muscle, being probably derived from the creatin which is formed there. Creatin represents an end-product of the metabolism of the *tissue protein* as distinguished from the nucleoprotein which arises chiefly from *nuclear material*.

These end-products of the metabolism of body tissues are spoken of as *endogenous*, and are constant in amount for the condition of the individual. They are increased or decreased by factors which vary metabolism, as fever, sleep, activity, etc. The same products, when resulting from the metabolism of food-stuffs containing the parent substances, are referred to as *exogenous*.

NUTRITION

The body is constantly liberating energy supplied by the food. The question to be discussed is, whether the different food-stuffs are of equal importance and whether they are all

necessary to the maintenance of life. It may be mentioned, in the first place, that digestion goes on more readily on a mixed diet.

In all experiments on nutrition it is necessary to keep an exact account of the amount and quality of both the food and the excreta. In this connection it is usually sufficient, as far as the proteins are concerned, to estimate the amount of nitrogen excreted in the urine and feces. Proteins contain by weight from 15 to 17 per cent. nitrogen, consequently the appearance of 1 gm. of nitrogen in the excreta indicates the decomposition of about 6.25 gm. of protein.

If the nitrogen excreted exactly equals the amount taken in the food, the animal is said to be in a condition of **nitrogenous equilibrium**. If the excreta contain less nitrogen than was taken in the food, nitrogen has been stored in the body; that is, protein has been laid up, **nitrogen retention**. If more nitrogen appears in the excreta than was contained in the food, the excess must have been derived from the breakdown of an unusual amount of body proteins.

Even if nitrogenous equilibrium is maintained, the weight of the body may not remain constant, for **carbon equilibrium** does not always accompany an equilibrium in nitrogen. To observe the fate of the fats and carbohydrates it is necessary to measure the amount of CO_2 excreted, since this is the chief end-product of the carbonaceous bodies. The ratio which exists between the amount of oxygen entering the lungs and the amount of CO_2 leaving them $\left(\frac{\text{CO}_2}{\text{O}_2}\right)$ is known as the **respiratory quotient**. This quotient indicates the extent to which the oxygen absorbed is used in the oxidation of carbon; This varies with circumstances—for example, with the diet. On a purely carbohydrate diet the quotient will approach unity, for sufficient oxygen is contained in the carbohydrate molecule to oxidize its hydrogen; on the other hand, a fatty diet will reduce the quotient, for in a molecule of, for instance, stearin, $\text{C}_3\text{H}_5(\text{C}_{18}\text{H}_{35}\text{O}_2)_3$, there are 110 atoms of hydrogen to but 6 of oxygen. The quotient

on a protein diet is intermediate between the two. During *starvation* the respiratory quotient falls, since the animal lives on its own store of fat and protein, the amount of carbohydrate in the body being very small. *Exercise* raises the quotient, owing to the fact that muscular work is done for the most part at the expense of carbohydrates.

Carbon is contained in all classes of food-stuff, and while a condition of nitrogenous equilibrium exists, glycogen or fat may be stored up even on a purely protein diet, leading to a deficit in the carbon excreted. On the other hand, fat or glycogen may be used up, and thus lead to the excretion of an excess of carbon without interfering with the maintenance of nitrogenous equilibrium. It is, therefore, necessary, in making experiments on the relative value or the fate of the food-stuffs, to estimate not only the nitrogen, but also the carbon of the food and excreta.

During *starvation* metabolism does not cease, but goes on entirely at the expense of the carbohydrates, fats, and proteins of the body. After using up a certain proportion of this store the animal dies, the period which lapses before death depending largely on the condition of the animal when starvation began. A lean animal will usually withstand the loss of about 0.4 of its body weight; one that is fat may live until its weight has been reduced by 0.5; an adult human being may live for three weeks without food if supplied with water; children die in a few days, after losing about 0.25 of their weight.

The glycogen of the muscles and liver is the first reserve store to be exhausted during starvation. Fat disappears rapidly; the proteins, as long as fat is being utilized, diminish very slowly. When most of the fat has been consumed the body falls back upon its store of proteins for the maintenance of temperature and for muscular work, and the excretion of urea is suddenly increased. While the fat lasts the proteins are not used to any extent as a source of energy, but when the supply of fat has been exhausted they must be so used. Even before this stage is reached protein must be

decomposed to form dextrose, which never disappears from the blood. As starvation progresses metabolism diminishes, and the loss of weight grows less from day to day. The greatest loss in weight is sustained by the adipose tissue; then come the muscles, next the liver, spleen, etc., and, lastly, the heart and central nervous system, which suffer almost no loss, for they live at the expense of the other tissues.

It might be supposed that a daily *supply of protein food*, equal in quantity to the amount of tissue protein which is broken down per diem during starvation, would suffice to keep an animal in a condition of *nitrogenous equilibrium*, but this is far from being the case. This depends upon the fact that protein metabolism within the cells is stimulated by the reception of protein food, the so-called *specific dynamic action* of protein. The larger the quantity of protein food which reaches the tissues, the more rapidly does protein metabolism go on, and, as a result of this, the cells are capable of using practically all the protein which is supplied to them. In one classic experiment a dog, during starvation, was found to consume his store of muscle at the rate of 165 grams per diem; at the same time he was burning up 95 grams of fat. His loss of weight was 260 grams daily. When given 500 grams of lean meat, the nitrogen in his urine showed that 599 grams were decomposed; that is, that he had used up 99 grams of muscle in addition to what he had received. At the same time 47 grams of fat were oxidized. The administration of 500 grams of meat only reduced his daily loss of weight to 146 grams. On gradually increasing the amount of protein food, from day to day, it was not until 1500 grams of meat were given that loss of weight was prevented; at this point nitrogenous equilibrium was established and 4 grams of fat were stored up. Increasing the amount of protein food still further did not lead to an appreciable storing up of protein tissue; in fact, when 2500 grams were given, 2512 grams were decomposed, a loss of muscle to the extent of 12 grams. Fat was, however, stored up to the

extent of 57 grams. Thus, if kept on a purely protein diet an animal must, in order to maintain nitrogenous equilibrium, receive a very considerable amount of food; if more than this be given, it does not lead to the storing-up of the excess, for the cells become spendthrift and burn up all the protein that they receive, in this way maintaining nitrogenous equilibrium at a higher level.

Protein metabolism may, however, be reduced by a **mixed diet**. In the case of the animal which required 1500 grams of meat for the maintenance of nitrogenous equilibrium, an addition of 150 grams of fat to this amount of meat resulted in the building up of tissue to the extent of 26 grams.

Moreover, when 150 grams of the fat were given, the amount of protein necessary for nitrogen equilibrium was much less; under these circumstances the allowance of meat was reduced to 800 grams without disturbance of the equilibrium. A mixed diet is, therefore, the most economic, for protein is the most expensive of foods; it is better physiologically, for digestion is much less likely to become disordered. Carbohydrates are even more effective than fats in the reduction of protein metabolism. If, then, it is desired to reduce protein metabolism as far as possible, in order that there may be a building up of tissue protein—of muscle, for example—it is best to give but a moderate amount of protein, with a mixture of the others.

The functions of food, to replace body tissue and to supply energy, cannot be fulfilled by either fats or carbohydrates alone no matter in what amount they are given, for the nitrogen of the protein molecule is necessary. An animal will die of **protein starvation**. There are, moreover, certain amino-acid groups within the protein molecule which are necessary for the reconstruction of new protein by the body. If an animal be fed upon protein deficient in one of these groups, it may continue in nitrogen equilibrium for a time, but will not grow or gain in weight. Gliadin, the protein from wheat or rye, is deficient in *lysine* and will not support growth. If, now, lysine be added to the diet, the animal will

proceed to grow. On a diet of mixed proteins it would be rare for this to happen, for what amino-bodies one protein lacks would be supplied by another. These very necessary bodies have been called **vitamins**.

Prolonged satisfactory maintenance may be obtained in man with a protein intake of from only 30 to 50 grams daily, provided sufficient fat and carbohydrate be given for the caloric needs. If left to himself, though, a man will choose a diet containing per diem approximately as follows:

Protein.	Fat.	Carbohydrate.
90-100 gm.	50-90 gm.	300-500 gm.

This probably takes into account unconsciously the bulk of food and the relative digestibility of the three food-stuffs.

Since we know the caloric value of each type of food we can calculate the energy requirement of the body. This, of course, varies with the intensity of the metabolism, but under average conditions is

For a man doing no work.....	2000 calories.
For a man doing moderate muscular work.....	2000 "
For a man doing hard muscular work.....	3500 "

Not only does the caloric need increase with muscular work, but the protein need also, for protein is needed for repair. Nevertheless, by far the greater part of the increased caloric value of the food will be obtained from carbohydrate and fat.

Exposure to cold also increases the general metabolism, and here again the increased demand is met by the non-nitrogenous food-stuffs.

Inorganic salts are just as essential a part of the diet as the foods which supply energy. It has been shown that an animal fed on food from which the inorganic salts have been as far as possible removed, will die sooner than a similar animal which is starved. The salts maintain the normal osmotic pressure in the liquids and tissues of the body; they

form a part of the molecular structure of protein; they are necessary for the normal irritability of living tissue; they maintain the globulins in solution; they maintain the alkalinity of the tissues. Certain salts have an especial interest: calcium for the part it plays in coagulation of blood and curdling of milk, sodium potassium and calcium for their effect on the rhythmic contractions of heart muscle and on the irritability of striate muscle.

A supply of **calcium** for the building up of bone is needed especially by growing children, and this want is particularly well supplied by milk, which contains an abundance of calcium. **Iron** is another substance which is needed, chiefly in relation to the formation of hemoglobin; this is supplied in combination with protein in the food, but inorganic salts of iron may be absorbed. A diet consisting entirely of milk is unsuitable for any but infants, for it contains an insufficient quantity of iron. The infant contains within its tissues a store of iron, which is slowly used up during the period of suckling; if confined to a milk diet beyond the usual time it becomes anemic.

Water supplies no energy to the body, but is indispensable, for in its absence metabolism is impossible. It composes 80 per cent. of the body by weight. It serves as a solvent for both food and excreta; in the removal of the latter, large quantities of water are eliminated and must be replaced. The evaporation of sweat is a most important means of resisting the effect of a high temperature.

ANIMAL HEAT

If a cold-blooded or, more properly, poikilothermic, animal is exposed to cold, its temperature sinks to that of its surroundings; on exposure to heat its temperature rises. Warm-blooded, or homiothermic, animals behave quite otherwise; their body tends to maintain itself at a constant temperature irrespective of the temperature of the surrounding medium.

The temperature of the body of a warm-blooded animal depends upon the liberation, in the form of heat, of the potential energy introduced in food. This is set free, mostly from the food that has been absorbed and assimilated, but to a less extent from the food as it undergoes digestion in the alimentary canal. Most of the body heat is *produced in the muscles*. Next to the muscles in heat production come the glands, more especially the liver. In order that the temperature may remain constant, as it does within very narrow limits, exactly the same amount of heat must be produced within the body as is given off from the surface and lost in the excreta. Both production and loss are very variable in actual amounts (the fuel needs of the body have been stated as varying from 2000 calories upward), but in the normal condition the one keeps pace with the other. During the rise and the fall of a fever this adjustment fails, though when the fever is maintained there is a caloric balance as in health. By means of a calorimeter large enough to contain the body, the amount of heat produced and given off may be determined. It is found to correspond very well with the fuel intake as determined by estimation of the caloric value of the food consumed. It increases with lowered temperature of the surrounding air, and with anything else which increases metabolism.

Muscular metabolism is the most readily varied of any in the body, and is the one called upon in emergencies. It is governed by the central nervous system, and the cells of the nervous system are subjected to afferent impulses coming from the periphery, for instance, from the skin. If **cold** be applied to the skin it reflexly causes the dispatch of efferent nerve impulses, which hasten the chemical changes within the muscles; more material is oxidized within the muscle and more **heat is produced**. If the cold be at all intense, the increased metabolism of the muscle will find visible expression in shivering, which consists of weak incoördinated contractions. The value of shivering is apparent. At the same time there occurs a **constriction of the**

cutaneous arterioles, brought about by reflex stimulation of the vasoconstrictor center from the afferent nerves of the skin. In consequence of this constriction less blood will flow through the superficial vessels, and the **loss of heat** will be much less than it would be were more blood brought near the surface. The animal will feel cold, owing to the cooling of the surface and peripheral terminations of the sensory nerves, which carry impulses toward the brain, but its temperature may, in reality, be a little higher than usual.

An animal whose spinal cord has been divided in the cervical region behaves as a cold-blooded animal; its metabolism is depressed by exposure to cold, increased by exposure to heat. The activity of the motor cells of the cord appears to be regulated by centers situated in some higher portion of the central nervous system, these latter centers being influenced by afferent impulses from the periphery.

When a warm-blooded animal is exposed to heat a constant body temperature is maintained, not so much by a lessened production of heat as by an *increased loss of heat* from the surface. The application of warmth to the skin brings about a reflex dilatation of the cutaneous vessels and secretion of sweat; the skin flushes, more blood being brought near to the surface. The sweat evaporates, and in the evaporation a large quantity of heat is absorbed from the blood and carried off, as latent heat, in the resulting water vapor. This is the most potent factor in preventing a rise of body temperature on exposure to a warm atmosphere. It will be readily understood that the cooling of the skin in this way will be materially influenced by the state of the surrounding air. If the air be dry, evaporation will be favored; if moist, retarded.

The effect of a hot bath is to raise the temperature of the body, for water is a much better conductor than air and will rapidly give up heat to the blood. At the same time, evaporation from the immersed skin will be prevented. A bath in water at 45° C. would soon prove fatal, while exposure to dry air at 125° C. might be borne with impunity

for the same length of time. The first effect of a *warm bath* is a slight rise of body temperature; after the bath is over there is a slight fall, but a return to normal soon follows. Although a *cold bath* abstracts much heat from the body, the metabolism is so increased that the first effect may be a slight rise of body temperature. If the bath be prolonged, a slight fall may result, but on leaving the water the temperature rises a little above normal.

Another factor of importance in the dissipation of heat is the raising of the temperature of the inspired air, and the evaporation by it of considerable water from the lungs. The relative importance of the different means of heat dissipation has been estimated, but we must bear in mind that high external temperatures diminish the loss by radiation and increase the loss by evaporation.

Loss in urine and feces.....	1.8 per cent.
Loss in expired air: Warming air.....	3.5 “
Vaporization of water.....	7.2 “
Loss by evaporation from skin.....	14.5 “
Loss by radiation from skin.....	73.0 “

The involuntary regulation of the body temperature may be voluntarily assisted by the donning or doffing of clothing, and by taking or abstaining from exercise. The **average rectal temperature** is about 37.2°C . (98.9°F .). Small daily variations occur, the temperature being lowest between midnight and early morning, highest in the late afternoon; the effect of a meal or of exercise is to slightly raise the temperature.

If a warm-blooded animal is exposed to such intense cold that the heightened metabolism cannot keep pace with the great loss from the surface, the temperature, after a preliminary rise, gradually sinks; unconsciousness supervenes, and is followed by death. The **hibernating** animals withstand the fall of body temperature, which may go almost as far as 0°C ., without ill effects. Metabolism proceeds at a minimal rate; the heart-beat is weak and infrequent; respiration is depressed and irregular, and the respiratory

exchange almost ceases. Cold-blooded animals may be frozen solid, and by gradual thawing be resuscitated; a snail has been reduced to a temperature of -120° C. without succumbing. In this case metabolism, of course, ceases; life becomes latent.

A warm-blooded animal poisoned with curari reacts to changes of temperature as though it were cold blooded. **Curari** paralyzes the terminations of the motor nerve-fibers, and thus deprives the central nervous system of its control over the chief thermogenic tissue of the body.

QUESTIONS FOR CHAPTER IX

During the absorption of carbohydrates, in which set of blood-vessels is the percentage of sugar the highest?

How may glycogen be most readily caused to disappear from the muscles?

Would you expect to cause glycosuria by puncturing the medulla of an animal which had for some time been fed on fat?

Is the appearance of sugar in the urine a necessarily serious symptom?

May it occur in health?

How is the percentage of sugar in the body increased after death?

How may we determine whether a certain substance is formed by a particular organ?

Compare the work done by the liver on a protein diet with that done on a carbohydrate diet.

Does sleep cause a variation in the rate of nitrogenous or non-nitrogenous metabolism?

Does all the urea which appears in the urine originate from the breakdown of tissue proteins?

From what nitrogenous substances may urea be formed by the liver?

What are the waste products of muscular metabolism?

Which is the more nutritious, soup made by boiling meat or the insoluble residue?

Which is the more palatable? Why?

Is the formation of fat from sugar a synthetic or an analytic process?

Mention instances of synthesis and analysis which occur during metabolism?

What different factors prevent an accumulation of sugar in the blood?

Is the percentage of ammonia in the urine increased by the administration of ammonium carbonate?

How may it be increased?

How may muscular exercise cause an increase in the excretion of urea?

If an animal receives no nitrogenous food, does nitrogen disappear from the urine?

What organ receives, in proportion to its size, the smallest arterial blood supply?

Do all the end-products of hepatic metabolism enter the bile-ducts?

Do the amounts of urea and uric acid in the urine always vary together?

What is the surest means of increasing protein metabolism?

If an animal be kept in a condition of nitrogenous equilibrium, does its weight necessarily remain constant?

Can an animal gain in weight when in a condition of carbon equilibrium?

Is it possible, by giving a large quantity of protein food, to cause the appearance of protein in the urine?

What is the final effect of an abundant diet containing an insufficient amount of protein?

Supposing that an animal is receiving a daily allowance of 200 gm. of protein food, and that it excretes 30 gm. of nitrogen and 60 gm. of carbon, what are we to conclude?

If an animal, on a diet of 200 gm. of protein, excretes 40 gm. of nitrogen and 120 gm. of carbon, what are we to conclude?

Under what circumstances will moderate muscular exercise cause a deficit of nitrogen in the urine?

Why does the administration of a mineral acid reduce the proportion of nitrogen which is excreted in the form of urea?

Under these circumstances, how is this nitrogen excreted?

During starvation the heart loses but little weight. Is the rate of cardiac metabolism slow as compared with that of skeletal muscle?

In choosing a diet for a child which is deprived of milk, to what inorganic constituent should special attention be paid?

What are the limitations to the use of milk as the sole article of diet?

What is the difference between the store of glycogen in the muscles and that in the liver?

What are the enzymes of the liver?

Is the liver of greater importance as an organ of digestion or of metabolism?

Which foodstuff is used by preference to obtain energy? Which next?

What becomes of an excess of carbohydrate food is eaten? What if fatty food? or protein?

What is the origin and significance of the acetone bodies?

In what tissues are the amino-acid bodies made use of, and how?

Are there other nitrogenous waste products than urea? How and where are they produced?

Is it important to distinguish between endogenous and exogenous origins of any metabolic products?

How do we determine the nitrogenous excretion? the carbon excretion?

What is meant by the term "vitamin"?

Give an average diet, showing the amount of the three foodstuffs to be taken per day.

What effect has muscular work on the dietary needs?

Since heat is being continually produced within the body, why does not the body temperature continually rise?

By what paths does the body lose heat?

What nerve centers are concerned in regulating the loss of heat?

How is the regulation of body temperature affected by the division of the afferent cutaneous nerves?

After this operation, will an animal better withstand exposure to heat or cold?

Compare the effect on the regulation of body temperature which results from division of the ventral spinal nerve-roots with that which follows division of the sympathetic rami communicantes. In the former case, what reflex which normally follows exposure to cold will be prevented, while in the latter case it persists? What cold and heat reflexes will be rendered impossible in each case?

In very hot weather, will the administration of atropin tend to raise or lower the body temperature?

Can we by means of the clinical thermometer determine the rate of heat production or heat loss?

Under what circumstances may the temperature of the body rise, while the production of heat remains constant?

Does a fall of body temperature always depend on lessened heat production?

The sensation of warmth which on a cold day results from drinking alcohol is due to the warming of the skin by an increase in the cutaneous circulation, the activity of the constrictor center being depressed by the alcohol. What is the effect on the temperature of the body as a whole?

CHAPTER X

SECRETION AND EXCRETION

SECRECTIONS are the products of the activity of specialized epithelial cells. The secretions of the *glands* of the *digestive tract* have been considered under that head, and it has been mentioned under metabolism that the **liver** produces and gives off to the blood directly two substances, glucose and urea. This latter sort of process, the direct setting free in the blood-stream of a glandular product, is designated by the term **internal secretion**. It has been also mentioned that the **pancreas** produces a substance which is necessary for the proper oxidation of glucose by the tissues. This is the internal secretion of the pancreas and is produced by the cells of the islands of Langerhans. In diabetes mellitus, where this secretion is considered to be absent, the cells of the islands are found atrophied.

The **thyroid gland** furnishes an internal secretion of much importance to metabolism. It is a colloid, produced by the lining epithelium of the vesicles. The active part seems to be a substance called *iodothylin*, which has a high iodine content and occurs in combination with protein. Its action, as ascertained by feeding gland tissue to normal animals and by observing animals with overactive glands (*exophthalmic goiter*), is to stimulate the metabolism of all the tissues and especially of the nervous system. The individual is overactive and nervous, heart and respiration are rapid, the skin is flushed, etc. Removal of the thyroid or its atrophy produces a condition known as **myxedema**; the general metabolism is lowered, the individual is sluggish physically and mentally, the skin is thickened, rather edematous, and loses the hair. A similar condition in infants due to deficient

functioning of the thyroid is characterized by these signs and by arrested growth as well. It is called **cretinism**. Partial removal of the gland decreases the symptoms of overactivity; feeding the gland corrects the myxedema or cretinism.

The **parathyroids** are of vital importance, since their removal is promptly followed by the development of what is called **tetany**. The symptoms are those of increased irritability of the neuromuscular apparatus: tremor, twitching, spasms, and convulsions. The animal dies shortly. Increasing the calcium salts in the blood by injection or by feeding will restore the animal, as will parathyroid feeding. The reasons for the symptoms are unknown, but two main theories are suggested: (1) the glands neutralize toxic substances formed elsewhere in the body; (2) they are concerned in calcium metabolism, deficiency in which causes the symptoms.

Thyroid and parathyroid in some way mutually influence each other's activity.

The **adrenals** (suprarenal capsules) also have a secretion of considerable importance, as shown by the fact that animals from which they have been removed show very marked symptoms leading to death. **Addison's disease** in man is accompanied by a destruction of the adrenal tissue, and the same symptoms: great prostration, muscular weakness, marked diminution of vascular tone, and a peculiar bronze pigmentation of the skin and mucous membranes. Feeding the gland or injecting it does not relieve these symptoms; the explanation of this being that in the first case the substance is destroyed by the digestive juices, while in the second case the injections cannot be made frequently enough to simulate the natural secretion. Injections of the gland substance are quickly followed by a rise in general blood-pressure, but this effect lasts only a few seconds and then subsides. Of the two parts of the gland, the medulla has been shown to contain the substance affecting blood-pressure. This has been isolated, and is called *epinephrin*. The medullary cells have an affinity for chromates, so that they may be stained

yellow by them. Such cells are also found in the sympathetic ganglia, and lying in clumps along the abdominal aorta. These *chromophil* or *chromaffin* tissues are the source of the body's supply of epinephrin. Epinephrin raises blood-pressure by causing contraction of the muscular coats of the arteries. It only contracts those arteries, however, which are supplied with vasoconstrictor fibers from the sympathetic system; not the vessels of the brain, or lungs, or coronary circulation. The action seems to be a stimulation of the neuromuscular junction of these fibers, for where stimulation of the sympathetic causes relaxation, as in the muscles of the intestine, epinephrin also causes relaxation. The continuous secretion of small amounts of epinephrin is considered necessary to the proper functioning of the sympathetic system. Besides its blood-pressure effect, epinephrin injection may produce a disturbance of the *carbohydrate metabolism*, so that hyperglycemia results. The cause of this is not understood, but if the glands are removed or diseased, carbohydrates can be tolerated in larger amounts than usual, so that alimentary hyperglycemia is more difficult to produce. It is as if the substance aided the conversion of glycogen to dextrose. No function has been demonstrated for the cortical portion of the gland.

The **pituitary body** (hypophysis) is made up of two distinct lobes, anterior and posterior. The posterior lobe has a lining of cells derived from the anterior lobe, which is called the *pars intermedia*. Complete removal of the *anterior lobe* is quickly fatal. Hypertrophy of the anterior lobe results in an overgrowth of the bony tissue of the body, recognized in man as acromegaly or gigantism, so that this internal secretion is supposed to influence the metabolism of growth and development, particularly of bony growth. Removal of the posterior lobe and *pars intermedia* is accompanied by drowsiness, low blood-pressure, high tolerance for carbohydrate, and storing of fat; symptoms suggesting those of hibernation, and not so unlike those of adrenal extirpation. Injection of extract of posterior lobe causes a rise in blood-

pressure like that of epinephrin, but more prolonged. It causes contraction of all smooth muscle tissue (intestine, uterus, dilator pupillæ, arteries, bronchi, etc.), and, like epinephrin, a lowered carbohydrate tolerance. This gland has also an augmenting effect on the development of the sexual apparatus.

The **pineal body** (epiphysis) is not well understood, but it appears to have an internal secretion which, as determined by the results of hypertrophy and of feeding experiments, tends to augment growth and the development of the sexual and mental functions. Such results can, of course, only be observed with young, growing animals.

The **thymus** is also obscure, but is believed to furnish something essential to the growth of young animals. Hyperplasia, or persistence in the adult, is accompanied by characteristic physical changes which might be summarized as a persistence of infantile characteristics; as if the secretion inhibited the development of the adult type.

The **gonads** (organs of reproduction) are considered to have an internal secretion which governs the sexual desire of the individual, seems to have a generally tonic effect, and in the female causes menstruation.

All of the glands of internal secretion have a close interrelation of action, so that changes in one are accompanied either as a result or as an attempt at compensation by changes in others. It will be noted as an example that thyroid, adrenal, hypophysis, and pancreas all have an effect on carbohydrate metabolism. The whole subject is very complex and needs further investigation.

EXCRETION

Besides the digestive and internal secretions which are useful to the body, there are certain other secretions which are formed for the purpose of ridding the body of a substance for which it cannot find further use, a waste product of metabolism. These secretions are extruded from the body and are called **excretions**.

The **bile** has been considered as a digestive secretion, but is also an excretion. The *bile-pigments* are waste products in the sense that they (1) are formed by the breaking down of the hemoglobin molecule; (2) have no function in digestion; (3) are cast off in the feces.

The *lecithin* and *cholesterin* are waste products of cellular life, and also are excreted in the feces. The *bile salts* (salts of glycocholic and taurocholic acids), besides having a digestive function, are reabsorbed in part from the intestines and act as cholagogues. The portion in the feces is one of the channels for the excretion of the sulphur of the protein molecule.

Bile-pigments are of especial interest because they are formed from the hematin radical of hemoglobin by splitting off the iron. The iron is mostly retained in the liver, presumably for further use, but the pigments, called **bilirubin** and **biliverdin**, are excreted. Some of the bile-pigment is reabsorbed from the intestinal tract, but none appears in the feces as such, being reduced in the intestines to a substance called **urobilin**.

The principal excretory channels are the urine and sweat, though the **lungs** form the channel for the excretion of carbon dioxide.

The **urine** is a yellowish, faintly acid liquid with an average specific gravity of 1020. A diet containing an excess of vegetables may cause it to be faintly alkaline because the organic acids are oxidized to carbonates. Besides water and inorganic salts the chief *constituents* of urine are urea, the purin bodies (uric acid and the xanthin bases), creatinin, hippuric acid, conjugated sulphates, and the urinary pigments. The origin of most of these substances has been already discussed. **Urea** is excreted to the amount of about 30 gm. per diem, the amount naturally varying with the protein metabolism. **Uric acid** is also very variable in amount, the average being about 0.8 gm.; the endogenous portion amounts to 0.15 to 0.2 gm., and the remainder, the exogenous portion, is the variable.

Free uric acid is not found in fresh urine; it is excreted

in the form of the more soluble urates; on standing, these may be converted into free acid, which is precipitated; this occurs most readily in acid urine, and is due to the reaction of the urates with the acid phosphates. The **xanthin bases** include xanthin, hypoxanthin, guanin, adenin, etc.; they are closely related to uric acid, which may be formed from them in the body. About 0.1 gm. xanthin bases is excreted per diem. The **creatinin** of the urine is derived chiefly from the creatin of the food, and varies with the amount so taken, the average excretion being about 1 gm. per diem. **Hippuric acid** occurs in the urine to the extent of about 0.7 gm. per diem, and varies with the amount of vegetable food eaten. The **conjugated sulphates** have been mentioned in speaking of protein putrefaction in the large intestine; conditions which favor the growth and activity of these putrefactive bacteria in the intestines increase the amount of these substances in the urine. The **urinary pigments** are derived directly or indirectly from hemoglobin. Not the whole of the **inorganic constituents** of the urine are derived directly from the food; for instance, sulphuric acid and phosphoric acid are formed in the metabolism of proteins, the sulphates of the urine originating, for the most part, in this way, the phosphates to a less extent. Besides sulphates and phosphates, there are present carbonates and, in larger quantity, chlorids. Sodium, potassium, magnesium, and calcium are present; the relative quantity of each is indicated by the order in which they are mentioned; they are, of course, combined as salts.

The **acidity of the urine** is not due to the presence of free acid, but to the acid phosphates, and to the acidity of its nitrogenous bodies excepting the urea. Both acid and alkaline phosphates are present in the urine, the former predominating. The degree of acidity depends upon several factors; in the main it represents the balance between the available bases taken in the food and the acids produced in metabolism. Vegetable food contains, in addition to alkalies, salts of organic acids, which, on oxidation, are con-

verted into carbonates, and may be used in neutralizing the acids formed during metabolism; vegetable food, therefore, reduces the acidity of the urine. From animal food, on the other hand, the amount of acid formed by oxidation of the sulphur and phosphorus of protein exceeds the available bases, and the excess is neutralized by the conversion of alkaline into acid phosphates.

The **specific gravity** varies from 1015 to 1025, and depends chiefly upon the amount of liquid absorbed by the alimentary canal and the amount excreted through other channels. The amount of food consumed will, of course, influence the quantity of solids excreted. To average the errors from these sources it is best, in making observations on the urine, to collect and mix the whole amount passed in twenty-four hours, beginning with an empty bladder. The **amount** varies from 1200 to 1700 c.c.

The secretion of urine depends chiefly upon the **blood-supply of the kidney**. The kidney receives this supply, through the short renal artery, from the aorta; the pressure in the first set of capillaries—those forming the glomerulus—being, in consequence of this arrangement, relatively high. The pressure in the capillaries of the kidney varies, of course, with the strength and rate of the heart-beat; it also varies with the condition of the arterioles in other parts of the body, and, in addition, with the state of its own arterioles. The kidney will receive the most abundant supply of blood when the heart-beat is strong, the vessels of other parts constricted, and the local arterioles dilated. Under these circumstances the amount of urine secreted will be abundant. In cold weather the cutaneous vessels are constricted and more blood flows through the abdominal organs, including the kidney; in cold weather, therefore, more urine will be secreted than when it is warm, for in the latter condition the kidney receives less blood, the skin more.

The kidney vessels are controlled by the central nervous system, through both **vasoconstrictor** and **vasodilator nerves** which leave the spinal cord in the lower thoracic nerves, enter

the sympathetic, and pass through the splanchnic nerves to the solar ganglia, where they probably end in contact with cells whose non-medullated axons (post-ganglionic fibers) pass along the renal artery to the kidney. A division of these nerves results in a dilatation of the renal arterioles and an increased flow of urine; their stimulation ordinarily causes vasoconstriction and lessened secretion, but if stimulated with slowly repeated induction shocks the action of the vasodilators is called into play.

We do not know precisely **how the urine is secreted**, but though a specific secretory activity has been claimed for the epithelium, the water and inorganic salts are probably filtered through the walls of the glomerular capillaries and epithelium of the **capsule**. The conditions are very favorable to **filtration**, for the blood-pressure in the capillaries is high and that in the capsule must be low, as there is a free exit for the urine through the tubules. The capsular epithelium may be supposed to act like a gelatin membrane through which the water and salts of blood-serum may be filtered, leaving behind the proteins. In such a case the resistance to filtration does not consist only in that offered by the membrane to the passage of water and salts, for the proteins, owing to the osmotic pressure which they exert, tend to retain water and to prevent its escape from the serum. The **proteins** of plasma exert an **osmotic pressure** of from 25 to 30 mm. of mercury; this, then, must be added to the resistance which is offered by the membrane to filtration of water and salts. Thus, to cause filtration a somewhat greater force is needed, and it has been found that the secretion of urine ceases when the general blood-pressure falls below 40 mm. of mercury; it also ceases when the pressure in the capsule has been raised to within 40 or 50 mm. Hg. of that in the capillaries. The filtration hypothesis has been disputed on the ground that ligation of the renal vein, while it must raise the intracapillary pressure and thus favor filtration, nevertheless puts a stop to the secretion of urine. This, however, may not be a valid objection, for the disten-

tion of the veins which results probably compresses the renal tubules, and by preventing the exit of the urine raises the pressure in the capsule toward that in the capillaries. Ligation of the renal artery will stop the flow of urine, but on releasing the ligature the flow does not start again for some time. This has been a strong argument against the filtration hypothesis, and cannot be explained on that ground at present, because an injury to the cells should make them *more permeable*.

The urine as it leaves the kidney is a very different liquid from any that could result from the mere filtration of blood-plasma; if, then, filtration goes on into the capsule, this filtrate must be greatly modified as it passes through the tubule toward the pelvis of the kidney. This undoubtedly takes place, for the more rapidly the urine passes through the tubules, the less it is modified, and the more it resembles the plasma in composition and reaction. When it traverses the tubules more slowly, time is given for its **concentration**, apparently by the absorption of water. If water is absorbed from the glomerular filtrate by the cells which line the tubule, they perform an immense quantity of work, for the osmotic pressure of the urine is much greater than that of the blood-plasma.

The cells of which the **convoluted tubules** are formed are much more highly developed than those which line the capsule, and we might expect them to be more specialized in function. It seems probable that the uric acid, urea, and the other more complicated nitrogenous substances which are secreted have this origin.

The urine as it leaves the capsule is alkaline, but while passing through the tubules its reaction is changed to acid by the addition of acid phosphates and certain organic acids (nitrogenous).

Diuretics are substances which increase the flow of urine. One type of diuretic action is shown by the saline diuretics, which act by bringing about a condition of *hydremic plethora*. Their high osmotic pressure attracts water into the blood

from the tissues, and this increased blood volume causes the flow of urine. All of the inorganic salts exhibit this action, but to a different degree in proportion to their osmotic pressure. Dextrose has a similar action, and it has been disputed whether urea acts thus also, or whether, as is more likely, it merely carries water with it as it is secreted by the cells of the tubules. Another type of diuretic action is by *dilatation* of the *renal arterioles*, and a third, by *stimulation* of the *secretory epithelium*.

The **ureter** carries the urine from kidney to bladder, somewhat aiding the flow by rhythmic contractions which sweep down the ureter every twenty seconds or so. These appear to be of muscular origin, since they may continue, after isolation, in the portions of the ureter which contain no nerve cells. The ureter, on reaching the bladder, runs for a short distance obliquely through the bladder wall. A valve is thus formed which prevents the backflow of urine from the bladder into the ureter, for a rise of pressure in the bladder will compress this portion of the ureter.

Micturition.—When the bladder contains no urine its muscular walls are in a state of slight tonic contraction; as urine enters, the muscles relax slightly, and, provided the urine is not introduced too rapidly, allow an accumulation of about 250 c.c.; when this point has been reached rhythmic contractions appear and increase in force as distention goes on. The exit of the urine into the urethra is prevented by the elasticity of the neck of the bladder and of the surrounding parts, and, perhaps, by a reflex tonic contraction of the circular coat of muscle at this point. As the bladder fills a desire to urinate is felt due to a slight leakage of urine into the prostatic portion of the urethra, occurring with one of the rhythmic contractions. At this point urination may be prevented by contraction of the band of voluntary muscle about the beginning of the urethra. If this does not occur, the bladder contraction forces the urine out through the urethra.

After division of the spinal cord in the thoracic region

micturition may still be carried on by the cells of the lumbar cord. The **bladder is innervated** by two sets of nerves; one set, leaving the cord in the fourth to fifth lumbar nerves, enters the sympathetic, and, reaching the inferior mesenteric ganglia, is here connected with ganglion cells from which originate postganglionic fibers, distributed to the bladder through the hypogastric nerve and plexus. Stimulation of these nerves excites weak contractions of the bladder wall. The other set of fibers leaves the cord in the second and third sacral nerves, and, without entering the sympathetic, reaches the hypogastric plexus through the *nervi erigentes*. These fibers end in small ganglia, situated in or near the bladder wall, where they come into contact relations with the cells whose axons form the postganglionic link in this chain. These nerves, when stimulated, cause strong contractions of the bladder and expulsion of the urine.

If the lumbar region of the spinal cord is destroyed, all nervous control over the bladder is lost, but in the dog the bladder empties itself at irregular intervals, a stimulus being afforded to the muscle by the stretching which results from distention; in man the urine accumulates in the bladder to a certain extent, and, after this, as the urine enters from the ureters, the excess drains off through the urethra.

SECRETION OF SWEAT

The sweat is a watery fluid containing but a small percentage of solid matter. Sodium chlorid forms the chief solid constituent; there are also present other salts, fatty acids, and traces of urea. The sweat is ordinarily acid in reaction, but if abundant is neutral or alkaline. In uremia the amount of urea is sometimes much increased. The amount of sweat secreted naturally varies considerably, being much greater in warm than in cold weather. Ordinarily, the sweat evaporates as fast as it reaches the surface; this is called invisible or insensible perspiration. The amount of insensible perspiration depends upon the condition of the

surrounding atmosphere; if the air be moist, less of the sweat will evaporate and the skin will be visibly damp; if the air be dry and warm, evaporation will go on more rapidly and the skin may appear dry, though the secretion may, in reality, be more abundant. When the skin is flushed the secretion of sweat is usually, but not necessarily, increased.

An abundant supply of blood to the sweat glands favors, but does not provoke, their activity, which is controlled by definite **secretory nerves**. These nerve-fibers leave the thoracic and upper lumbar regions of the spinal cord and end in the ganglia of the lateral sympathetic chain; the post-ganglionic fibers, which arise from cells in these ganglia, pass through the gray rami to the various spinal nerve-trunks, and are distributed through the cutaneous branches of these to the sweat glands. The course is similar to that followed by the vasoconstrictors. The preganglionic sweat nerves for the skin of the face and head end in the superior cervical sympathetic ganglion. It is not known whether there exists in the medulla a chief sweat center to which the spinal sweat centers are subordinate.

The sweat centers are stimulated by a rise in the temperature of the blood, and also by increased venosity. Sweat may also be secreted as a result of the emotions; in such cases the spinal centers are stimulated by involuntary nerve impulses descending from the brain; they cannot be voluntarily controlled. The secretion of sweat is ordinarily a **reflex** event arising from the stimulation of afferent cutaneous nerves, as by the application of heat. That it is not a result of the direct stimulation of the glands by heat is shown by the fact that exposure to heat, after the division of the nerves of a part, does not cause sweating of the paralyzed area. At the same time, the impossibility of provoking the secretion by increasing the blood supply is demonstrated, for, owing to the division of the vasoconstrictors, the skin will be flushed, yet it will remain dry. Stimulation of the peripheral end of the divided nerve, although it will bring about a paling of the skin, through the stimulation of the vasocon-

strictors, will cause sweating of the part by exciting the sweat nerves.

The **sebaceous glands** of the skin have not been shown to be controlled through the nerves. The sebum excreted by these glands consists of the débris which results from the degeneration of the epithelial cells of the glands themselves. It is an oily liquid made up of fats, fatty acids, cholesterin, protein, salts, and water.

THE SECRETION OF MILK

Unlike the sebaceous and sweat glands, to which it is nearly related, the mammary gland is only occasionally active; in the male, with very infrequent exceptions, never. That the activity of this gland may, to a certain extent, be influenced by the nervous system is proved by the frequent instances of the cessation or modification of lactation as a result of emotions or nervous disorder. There is, however, little or no experimental evidence from which we can gain an insight into the mechanism.

Milk consists chiefly of water, holding in solution proteins, carbohydrates, and inorganic salts, and in suspension, globules of fat. The chief **protein** is caseinogen, a nucleo-albumin; in addition, there are smaller quantities of albumin and globulin. Lactose is the chief **carbohydrate**, and occurs in larger amount than the caseinogen. The **fat** consists of stearin, palmitin, olein, and smaller quantities of other fats. The inorganic constituents, with the exception of iron, closely correspond, in the proportion which they bear to one another, to those of the newborn animal.

The average proportions of the constituents of normal human milk and cows' milk are as follows:

	Human. Per cent.	Cows'. Per cent.
Fat.....	4.0	4.0
Sugar.....	7.0	4.5
Proteins.....	1.5	3.5
Salts.....	0.2	0.75
Water.....	87.3	87.25

Before lactation begins the alveoli of the gland enlarge, the epithelium thickens, and the cells multiply. There appear within the cells, more particularly near their free border, granules and fat droplets which are extruded into the alveoli. At the beginning of lactation for a day or two the secretion varies from that which follows, in having numerous degenerated cells, a lower percentage of fat and sugar and almost four times as much protein. The effect of this early secretion, which is called **colostrum**, is to cause a free evacuation of the bowels of the nursing child. Colostrum is lacking in caseinogen, in spite of its high protein percentage.

The normal physiologic stimulus to the activity of the gland cells is the emptying of the ducts, and although up to a certain point the secretion is continuous without external stimulus, when the alveoli and ducts are distended secretion is inhibited reflexly or directly by the high pressure in the ducts, to be resumed, and at a very rapid rate, when the child nurses. The activity of the gland varies with the physical stimulus of the sucking child. The amount varies under normal conditions from 10 to 16 ounces a day in the first week of lactation to 30 to 40 ounces a day in the ninth month of lactation.

In an average nursing period of ten to twenty minutes, the amount obtained from a single breast varies from about 1 ounce in the first week to 6 ounces in the sixth week and later. Lactation usually ceases promptly when nursing is discontinued, but the application of pressure and cold and the use of atropin and saline cathartics hasten the cessation of the glandular activity and the process of involution in the gland.

The proteins of the diet if in excess increase the protein caseinogen of the milk, also the fat and possibly the sugar. Lack of exercise will have the same effect as excessive protein diet. The percentage of fats, carbohydrates, and proteins in the milk can be easily diminished by a free fluid diet.

QUESTIONS FOR CHAPTER X

How does an internal secretion differ from an external secretion?

Contrast the importance of the internal and external secretions of the pancreas.

What are the internal secretions of the liver?

What is the relation of the thyroid gland to myxedema, cretinism, and exophthalmic goiter?

Are the parathyroids of much importance? If so, in what way?

In what part of the adrenals do we find the active principle?

Name the two important actions of epinephrin.

How can we distinguish between hypertrophy of the two lobes of the pituitary body?

What other organs have an internal secretion?

Name the excretory channels.

What is the metabolic importance of the bile-pigments?

Name the most prominent differences between the composition of the blood-plasma and of the urine.

What readily diffusible substance is found in the blood, but not in the urine?

Compare the effect of dividing the renal nerves with that of stimulating them—(a) in regard to the renal blood supply, (b) with respect to the secretion of urine.

Why is the amount of uric acid excreted more variable than the urea?

What is the chief difference between the action of the glomerulus and the tubule?

Describe the mechanism of urination.

Where is the center which controls urination?

Make a similar comparison of the effects of dividing and stimulating the sciatic nerve on the blood supply and activity of the sweat glands of the leg?

Compare the nature of the control exercised by the nervous system, on the one hand, over the secretion of urine, on the other, over the secretion of sweat?

Under what circumstances may the quantity of urine in health fall considerably below the average?

What effect have the seasons on the specific gravity of the urine?

How do you collect twenty-four-hours urine?

Why does the injection of a large quantity of normal saline solution into the vessels cause diuresis?

Supposing that the sodium chlorid of the plasma were incapable of passing from the glomerulus into the capsule, would the blood-pressure required for the filtration of water be greater or less than the normal?

How do you account for the fact that the urine is, in respect to inorganic constituents, more concentrated than the plasma?

Would you expect the reaction of the urine to vary with its specific gravity? Why?

What effect has the administration of alkalis on the relations existing between different nitrogenous compounds of the urine?

What is the simplest method of producing diuresis?

Which of the normal constituents of the blood-plasma, when present in excess, cause diuresis?

How would the secretion of urine be affected by increasing the percentage of proteins in the blood-plasma?

How may the reaction of the urine be caused to resemble that of the blood?

How does starvation modify the urine of the herbivora?

What relation exists between the amount of blood supplied to the kidney and the reaction of the urine?

How may we determine whether a drug which exerts an influence over the secretion of sweat acts upon the sweat centers or on the peripheral mechanism?

How may we determine whether, on application of heat to the skin, the sweat glands are stimulated directly or reflexly?

What are the reasons for the intermittent function of the mammary glands?

Describe the normal course of lactation.

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